PHYSIOLOGICAL RESPONSES, FACIAL EXPRESSIONS, AND CRY OF INFANTS DURING IMMUNIZATION IN RELATION TO THEIR PAIN HISTORY

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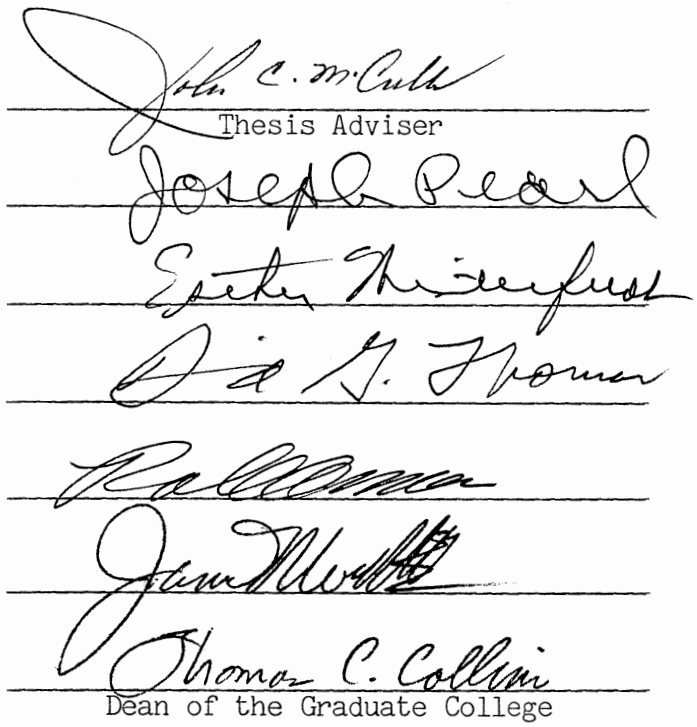

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Physiological Responses, Facial Expressions, and Cry of Infants During Immunization in Relation to Their Pain History

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This study is based on the doctoral dissertation research of the first author under the supervision of the second author and was partially funded by grants to the first author from the National Association of Pediatric Nurse Associates and Practitioners Foundation, the Zeta Delta Chapter of Sigma Theta Tau, and the Oklahoma Nurses Foundation.

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Abstract

This study examined infants' physiological and behavioral responses to an injection and the relationship between these responses, and the effect of previous painful experiences on infants' responses to present pain in 105 healthy infants in five age groups, 2, 4, 6, 15, and 18 months. Changes in heart rate, oxygen saturation, cry, and facial expression were analyzed from videotaped records; pain history was assessed using the Infant Pain Inventory.

The results showed that anger expressions occurred more frequently with increasing age. However, experience also affected facial expression. The majority of children receiving two injections displayed physical distress expressions immediately after the first injection, but more children displayed anger expressions after the second one. Subjects with high pain history scores relative to those with low scores displayed significantly more physical distress or anger expressions. A U-shaped developmental trend was found in which youngest and oldest subjects had higher increases in heart rate, longer times to minimum oxygen saturation, and were least likely to soothe. Facial expression most consistently indicated pain, but duration of cry was a better measure of behavioral soothing. Heart rate showed a rise above baseline in almost all subjects and the change was smaller in soothed children. Oxygen saturation data generally were not useful. Behavioral measures (cry and facial expression) returned to baseline before the physiological measure of heart rate.

Physiological Responses, Facial Expressions, and Cry of Infants During Immunization in Relation to Their Pain History

Until recently, the recognition, assessment, and treatment of pain in infants received little attention (Fitzgerald, 1987). It has long been thought that because nerve pathways are not completely myelinated at birth, infants do not experience pain or remember painful events (Swafford & Allen, 1968). However, this view is currently being challenged as neural transmission of pain has become better understood and as better measurements of pain responses in infants have been developed. (Refer to Appendix A for an extensive review of this literature.)

Despite this expanding body of knowledge, many health professionals continue to maintain that infants as old as two years of age do not experience pain similar to adults, and they may withhold analgesics and anesthetics, believing that such pain reducers are unsafe (Schechter & Allen, 1986). These traditional beliefs and fears have resulted in infants undergoing numerous painful procedures, including surgery, with little or no pain control (Anand & Ansley-Green, 1985; Bauchner, May, & Coates, 1992; Schechter, Allen, & Hanson, 1986). Similar practice with adults would be considered barbaric, inhumane, and unethical. Therefore, additional research on infant pain is needed to refine present knowledge and to address some unanswered questions, such as the relationship between various pain measures and the influence of the infant's previous experience with pain on these measures.

If it becomes generally conceded that infants experience pain, we may find that such experiences in the course of medical treatment are

both unnecessary and detrimental. For example, although little is known about the psychobiology of childhood stress, preliminary evidence suggests that physiologic responses to stressors, such as pain, may alter or initiate pathologic events that lead to clinical disease (Boyce, Barr, & Zeltzer, 1992). Thus, better knowledge about infant pain may lead to practices that control pain and ultimately benefit children.

The evaluation of pain in infants is difficult because pain is a subjective experience, operationally defined as "whatever the experiencing person says it is, existing whenever he says it does" (McCaffery & Beebe, 1989). Because this definition cannot be applied to infants, we need to examine nonverbal responses. Logically, whatever is painful to an adult should be painful to an infant if the infant responds behaviorally and physiologically to noxious stimuli as an adult does.

In terms of the development of the capacity for nociception (neuronal transmission of noxious stimuli to the spinal cord and thalamus), newborns have the anatomic and functional mechanisms required for the perception of pain (Anand & Hickey, 1987). Nociceptive nerve endings are present in all cutaneous and mucous surfaces by the 20th week of gestation. Neurotransmitters, such as substance P, and their receptors appear in the spinal cord at 8 to 14 weeks of gestation (Anand & Carr, 1989). Complete myelination of the pain pathways to the brain stem, thalamus, and cortex occurs by 37 weeks gestation. Before this time, incomplete myelination merely implies a slower conduction velocity in the nerves of infants, which is offset by the shorter interneuron and neuromuscular distances

traveled by the impulse. By 20 weeks gestation the cortex has a full complement of neurons, making physiologic detection of pain possible (Anand & Hickey, 1987). However, some inhibitory pathways do not develop until after birth, suggesting that premature infants may not only be capable of experiencing pain, they may be particularly sensitive to it (Stevens & Johnston, 1992).

Numerous studies have investigated infants' physiological and behavioral responses to medical procedures, such as circumcision and major surgery, that adults would obviously consider painful without anesthetics. Several physiological indices of pain, most of them observed in adults, have been documented in infants, such as increases in heart rate, blood pressure, respiratory rate, palmar sweating, stress hormones; decreases in blood oxygenation and vagal tone; and wide fluctuations in intracranial pressure (Anand & Hickey, 1992; Harpin & Rutter, 1983; Johnston & Strada, 1986; Lewis & Thomas, 1990; Porter, Porges, & Marshall, 1988; Stang, Gunnar, Snellman, Condon, & Kestenbaum 1988; Stevens, 1991; Williamson & Williamson, 1983).

Behavioral indices, including behavioral state (Dixon, Synder, Holve, & Bromberger, 1984; Marshall, Stratton, Moore, & Boxerman, 1980), cry (Porter, Miller, & Marshall, 1986; Grunau & Craig, 1987), movement (Franck, 1986; Johnston & Strada, 1986) and facial expression have also provided evidence for the existence of pain in infants. Facial expression has been found to be a specific and consistent indicator of infant pain (Dale, 1986; Grunau & Craig, 1987; Izard, Hembree, Dougherty, & Spizzirri, 1983; Izard, Hembree, & Huebner, 1987; Johnston & Strada, 1986). Although several systems exist for coding and interpreting facial expressions (Grunau & Craig, 1987;

Izard & Dougherty, 1982), differential emotions theory (Izard, 1977) permits facial expressions to be differentiated into two categories that theoretically represent the emotions of physical distress and anger. The theory also suggests that in normal development, new emotional expressions, such as anger, indicate higher level adaptive responses than expressions of physical distress and are more the result of maturation than experience.

Despite the number of studies that have investigated physiological and behavioral indicators of pain in infants, only a few have explored the relationship between these variables. Gunnar, Fisch, and Malone (1984) found that infants given a pacifier during circumcision without anesthesia had 40% less crying than a group without a pacifier, although both groups had similar cortisol elevations. Others have found that facial expression and/or cry return to a nonstressed state before heart rate returns to baseline (Johnston & Strada, 1986; Williamson & Williamson, 1983). These studies suggest that changes in behavior do not necessarily mirror underlying changes in physiology. Therefore, caution is needed when using a single indicator of pain.

Few investigators have compared the pain responses of infants at various stages of development, and none have attempted a comprehensive simultaneous analysis of behavioral and physiological responses. Our knowledge about developmental trends in young children's responses to pain is based largely on the early work by McGraw (1941), although there has been more a recent investigation by Craig, McMahon, Morison, and Zaskow (1984).

The general purpose of the present study was to add to our

existing knowledge and theoretical understanding of infant pain. The specific research questions were: (1) what are the physiological (heart rate and oxygen saturation) and behavioral (cry and facial expressions) responses of infants to pain, (2) what is the relationship among these responses, and (3) what is the effect of infants' prior painful experiences on present responses to pain? The "pain" stimulus used to evoke physiological and behavioral responses was injection of a vaccine, since it is generally accepted that verbal children and adults experience the procedure as painful. The hypotheses were that (1) there will be an increase in heart rate and a decrease in oxygen saturation, accompanied by crying and facial expressions of physical distress and/or anger during an immunization injection; (2) behavioral responses will return to baseline sooner than physiological responses; (3) infants with high pain history scores will demonstrate heightened and prolonged behavioral and physiological responses to pain, including greater anticipation of pain, than infants with low pain history scores; and (4) infants with high pain history scores will demonstrate a facial expression of anger at an earlier age than infants with low pain history scores. A final goal was to examine these findings in light of differential emotions theory.

Method

Subjects and Design

This study used a non-experimental design and a non-randomized convenience sample. The subjects were 115 children who were receiving immunizations as part of their routine health care at a private pediatrician's office (n = 13) or a county health department (n = 102)

in Tulsa, Oklahoma. Eligibility criteria for the children to be included in the sample were normal gestational age and weight at birth; close to the age at which immunizations are recommended for children under 24 months; actually immunized at time of visit; healthy at time of immunization; and developmentally normal in terms of the developmental screening. Because of equipment and recording problems (e.g., loose electrodes or sensor, weak oximeter or video camera battery, child's face or monitor display not clearly visible on the videotape), 10 subjects were lost from the sample.

Initially, the plan was to sample 3 groups of 30 infants each at three ages: 2, 6, and 18 months. These ages represent some of the recommended times for administration of the diphtheria, tetanus, and pertussis (DTP) vaccine (American Academy of Pediatrics, 1991). However, the data were collected during February 1990 following a measles outbreak in Oklahoma. Parents were encouraged to bring children under 2 years of age to a health care facility to update their children's immunizations, especially for measles. Consequently, large numbers of children were brought to the county health clinic for DTP, measles-mumps-rubella (MMR), and Haemophilus influenzae type B (Hib) vaccines. The final sample of 105 children clustered into 5 age groups. The age, gender, and ethnicity of these groups are summarized in Table 1. With five different age groups it became possible to

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Insert Table 1 about here

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consider developmental trends in infants' responses to pain that had not been specifically addressed in the original research questions.

Instruments

Several instruments were used to collect data both before and during the immunization. Before the vaccine was given, the infant's pain history and demographic data were collected by means of the Infant Pain Inventory (IPI) and the Parent Interview. To be certain that the child's chronologic age reflected his or her developmental age, the subject's developmental status was tested using the Revised Denver Prescreening Developmental Questionnaire (R-PDQ). Two (sometimes only 1) baseline apical heart rates were measured with a stethoscope. Copies of the IPI, the Parent Interview, and the R-PDQ are included in Appendix C.

During the administration of the vaccine, heart rate and oxygen saturation were continuously monitored electronically using oximetry. The values for these two variables and the child's crying were continuously recorded on videotape for the entire injection and postinjection periods (a total of three minutes). Facial expression was continuously recorded for the entire injection and part of the postinjection periods.

Pain history and demographic data. Both the IPI and the Parent Interview were developed specifically for this study. The IPI was designed to assess infant pain experiences across four categories: (1) Prenatal to Birth, (2) Postnatal Medical Procedures, (3) Sources of Postoperative Pain, and (4) Common Postnatal Health Conditions and Injuries. IPI items were obtained from children's reports of painful experiences during hospitalization (Wong & Baker, 1988), the investigator's personal professional experience with infant care, and a survey of 20 pediatric nurse experts.

The Parent Interview is a semi-structured interview designed to obtain basic demographic information about the child, specifically birth date, sex, race, type of delivery, past and current health history, and a general impression of the parent's perception of the infant's prior painful experiences.

Developmental screening. The developmental status of the infants was assessed using the Revised Denver Prescreening Developmental Questionnaire (R-PDQ). The R-PDQ uses a subset of questions from the full Revised-Denver Developmental Screening Test (R-DDST) for each age group (0-9 months, 9-24 months, 2-4 years, and 4-6 years) and takes 2 to 5 minutes to complete. The form is completed by having the parent answer a series of "yes" or "no" questions until 3 "no" responses are chosen. The responses are coded for those items a child is expected to perform. Children with no "delays" (item passed by 90% of children at a younger age than the child being screened) are considered to be developing normally. Test-retest agreement over a one-week period has been reported as 94.1% and inter-observer (parent-teacher) agreement as 83%. The R-PDQ has been found to identify 84% of nonnormal R-DDST results (Frankenburg, Fandal, and Thornton, 1987).

It was planned to administer the full R-DDST to all children with one or more delays on the R-PDQ. The R-PDQ was administered by a research assistant who reviewed all answers with the parent. When "no" responses were given for an item the child was expected to be able to perform, the research assistant checked to see if the child could actually perform the skill, such as head control or rolling over. With this type of administration, all children passed the R-PDQ screening test, and it was not necessary to give the full R-DDST to

any child.

Behavioral measurements. The behaviors measured were duration of crying and type of facial expression. These were recorded on videotape for later analysis. Crying was the typical distress vocalization, characterized by a pattern of loud high-pitched cry, often followed by a period of no breathing (apnea), with dysphonated cries (heard as grating, shrill, and tense), and a gradual return to the rhythmic rising-falling pattern. Soft cries without these characteristics were defined as whimpers.

The infants' facial expressions were scored by means of a modified Maximally Discriminative Facial Movement Coding System (Max), an anatomically based system for identifying nine emotional expressions of infants and young children (Izard & Dougherty, 1982). The Max rests on the assumption from differential emotions theory (Izard, 1977) that emotion activates organized patterns of facial movements and that facial expressions reflect the underlying emotions of human experience. Facial changes are objectively evaluated in three areas: (a) forehead/eyebrows/nasal root, (b) eye/nose/cheek, and (c) mouth/lips/chin. Criterion-related or predictive validity as measured by the agreement of untrained subjects' judgments of facial expressions of infants using the Max has been found to be 59.1% (Izard & Dougherty, 1982).

In this study, the Max was modified only in the respect that facial expressions were scored by stop-framing the videotape as many times as needed to identify the composite facial changes associated solely with physical distress and anger. Izard, Hembree, Dougherty, and Spizzirri (1983) found that in the first 10 seconds following an

immunization injection, 34 of 36 subjects showed only facial expressions of physical distress and/or anger. The facial expressions of physical distress and anger both consist of lowered brows that are drawn together; bulging, vertical furrows in the forehead between the brows; a broadened and bulging nasal root, and an angular, squarish mouth. The facial expressions of distress and anger differ only with respect to the eyes, which are kept open in the case of anger, but are fissured and tightly closed in the case of distress. If any one of the anatomic features were not seen, the facial expression was coded as no physical distress or anger. Interobserver reliability was established by having a trained observer and the investigator score the videotapes for 10 infants independently. This resulted in 90% agreement on facial expressions of physical distress and anger. However, the first author scored all of the videotapes.

Physiological measurements. Heart rate and oxygen saturation were measured continuously using a pulse oximeter. Two baseline apical heart rates were also taken with a stethoscope: one in the waiting room and the other before the oximeter was attached. The average of these two heart rates was used as a baseline measure. For 10 subjects, it was not possible to obtain a heart-rate measurement in the waiting room (usually because of time constraints); in these instances the measurement obtained before the oximeter was attached was used as the baseline heart rate. The accuracy of the oximeter is reported to be between 1 and 2% when oxygen saturation is in the range of 70 to 100% (Kulick, 1987). As blood oxygen saturation decreases, the error in accuracy averages about 5% (Hannhart, Haberer, Saunier, & Laxenaire, 1991).

Movement can affect the oximeter's accuracy. Since movement during the injection was expected, the Nellcor N-200 oximeter was chosen because it uses "C-Lock" electrocardiographic (ECG) synchronization, which reduces motion artifact and gives saturation readings within 2% of values obtained from a sensor placed on an immobilized hand (Barrington, Finer, & Ryan, 1988).

Initially, it was planned to record blood pressure also through automatic noninvasive monitoring via oscillometry. However, with the equipment available (the Dinamap oscillometer), accurate blood pressure measurement could not be obtained during the injection procedure and this measure had to be eliminated from the study.

Recording apparatus. A Minolta Master V1400 VHS camcorder was used to record facial expressions, cry, and instrument readings of heart rate and oxygen saturation. An RCA CGA030 character generator was used to superimpose time, date, and stopwatch functions on the videotape. Stopwatch functions provided elapsed time continuously on the tape in hundredths of a second. The scoring of the videotapes was facilitated by use of a Sony VCR SLV686 video cassette recorder with remote control that permitted stop framing and slow motion.

Procedure

The data were collected by the investigator and an assistant (both of whom were female doctoral students and masters-prepared registered nurses); a professional photographer videotaped the injection and postinjection events. The assistant worked with parents and infants in the clinic or pediatrician's waiting room to collect preinjection data. Specifically, she reviewed each subject's eligibility for inclusion in the study, discussed the study with

parents whose children were selected, obtained informed consent from the parent, collected pain history and demographic data, administered the R-PDQ, and measured baseline heart rate. Because the literacy level of the parents was not known, she reviewed each section of the forms verbally with the parent. For parents who did not speak English, Spanish and Chinese interpreters were available to translate. Less than 10% of parents used the interpreters. She initiated a form that identified the child by code and gave age in months, scheduled vaccine, baseline heart rate (if obtained), and status of completed forms. The parent retained this form until the child was ready to receive the injection, at which time the form was attached to the oximeter for identification and video recording purposes.

Following this period in the waiting area, the child and family members entered the examination room of the pediatrician's office or the immunization room of the clinic where the investigator and photographer, both blind as to the subject's pain history, collected the remaining research data. Each child first received an examination by the pediatrician or by a pediatric nurse practitioner in the clinic. Once the child was ready to receive the injection, the investigator explained the procedure for monitoring the child's heart rate and oxygen saturation using the oximeter, the necessary position of the child for the face to be videotaped, and the injection-postinjection events. Before the equipment was attached to the child, the second baseline heart rate was taken. The three electrodes were then attached to the chest, and the oximeter sensor placed around the big toe. To secure the equipment and minimize the artifact of movement, the sensor was taped to the toe and the wire connecting the

sensor to the monitor was secured to the sole of the foot using a self-adhering band placed around the entire foot. Hydrogel electrodes were used to provide a satisfactory adhesive with a nearly painless removal. Finally, the sock was replaced to cover the sensor, and the child's shirt was used to cover the electrodes.

Once the equipment was secured to the child, the oximeter was tested and the alarm was silenced to avoid possible distress to the family should heart rate or oxygen saturation exceed programmed limits. In order to facilitate videotaping of both the child's facial expression and readouts from the oximeter, the investigator held the oximeter near the child's face. For the data to be usable, the videorecording had to clearly show the child's face and the oximeter displays of heart rate and oxygen saturation.

In the pediatrician's office, the child was placed supine on an examination table, and the injection was given by one of three registered nurses. The parent was nearby and in some cases helped restrain the child. In the clinic, the child sat in the parent's lap, and the parent restrained the child for the immunization. A licensed practical nurse gave all of the injections. The parent was asked to keep the child's face toward the camera throughout the injection period and for 30 seconds afterward following the application of a bandaid to the injection site.

Since it was not always possible to videotape the injection procedure as well as the face, each step of the injection was noted orally by the nurse or investigator and recorded on tape. The words spoken at each step of the injection procedure were (a) "wipe," when wiping the injection site with alcohol began; (b) "in," when the

needle entered the skin; (c) "inject," when the syringe plunger was pushed to inject the vaccine; (d) "out," when the needle was removed; (e) "wipe," when the injection site was wiped with a dry cotton ball; and (f) "bandaid," when the bandaid was placed over the injection site. A total of 17 children, aged 15 to 21 months, received two injections during the visit. In this case, the nurse had two syringes prepared and immediately after giving the first injection gave the second injection. Both injections were videotaped, with the 30 second postinjection period beginning after the second injection. The vaccines received in each age group are presented in Table 2.

Insert Table 2 about here

All nurses used the same injection procedure. DTP or Hib (each 0.5ml) were administered intramuscularly in the anterolateral upper thigh (vastus lateralis muscle) using a 22 gauge, 1" needle. When two injections were given, separate legs were used for each and DTP was always given last. MMR (0.5ml) was administered subcutaneously in the upper arm (deltoid muscle) using a 25 gauge, 5/8" needle.

When the bandaid (or second bandaid) was applied, the investigator reminded the parent that the child's face would continue to be videotaped for an additional 30 seconds. When the 30-second period ended, the parent was informed that he or she could comfort the child. After this time only the oximeter display was videotaped. Any soothing measures the parent offered the child were also recorded. Most parents in the clinic chose to turn the child on their shoulder for comforting, and all parents in the pediatrician's office removed

the child from the examining table and held the youngster. A few parents gave the child a pacifier or a bottle of milk or juice. Initially, the plan was to videotape the child's face for three minutes. However, in a pilot study, parents refused to refrain from comforting their child for this length of time. Thirty seconds was about as long as most parents could keep their child's face on camera, and refrain from comforting.

Videotaping began when the skin was wiped with alcohol and continued for at least 30 seconds. Once videotaping was completed, all equipment was removed, and parents and children were thanked for their time and cooperation.

Scoring

Measures of heart rate (beats/minute) and oxygen saturation (percent) were taken from the oximeter display on the videotape. Loud crying and whimpering were scored from the audio portion of the videotape. Facial expressions as seen on the videotape were coded as physical distress or anger based on the anatomical descriptions in the Max.

All measures were transcribed for analysis beginning with the first "wipe" step of the procedure. However, the "in" step was chosen as the zero point for data analysis because it represented the point at which the noxious stimulus was applied. The duration of the injection from "in" time to applying the bandaid averaged 11.5 seconds (SD = 3.64 seconds). When the injection procedure was visible on the tape, the steps were identified from the video portion of the tape; otherwise they were identified from the audio portion of the tape. Measures were also recorded at each 5-second interval for the

remainder of the first 60 seconds, and at each 10-second interval afterward until the end of the observation period. Some data were recorded more frequently to answer specific questions. For example, to plot the normalized heart rate, the heart rate was recorded every 5 seconds until it returned to baseline or the 3-minute videotaping was completed, whichever occurred first. During analysis of the videotapes, the first author viewed each frame repeatedly to identify the clearest facial expression and oximeter displays for that time interval.

Results

The results are presented in relation to the three research questions. Not all subjects were included in every data analysis. Some had missing data. Some were crying before the injection was given, making some measurements, such as time to initial cry, meaningless. Some did not meet criteria for analysis; for example, time to pulse soothing required that heart rate return to baseline within three minutes. Nevertheless, some usable data for analysis purposes were obtained on all 105 subjects. Since group comparisons included different numbers of subjects, in all analyses of variance (ANOVA) the methods employed were those for unequal number of replications. Summary tables of sex and race data are in Appendix E.

Physiological and Behavioral Responses to Injection

Data analyses were performed on heart rate, oxygen saturation, cry, and facial expression. Results are presented for each variable.

Heart rate. Four separate analyses of heart rate were performed: (a) trend in normalized heart rate, defined as ratio of instantaneous heart rate to baseline heart rate; (b) maximum fractional increase in

heart rate, defined as the heart rate minus baseline heart rate divided by baseline heart rate, which reflects percentage increase from baseline; (c) time in seconds to reach maximum heart rate; and (d) time to pulse soothing, defined as time in seconds until heart rate returned to baseline rate.

For 10 subjects only the second baseline heart rate was obtained, and was used as the baseline rather than an average of two baseline rates. A t test, $t(150) = 1.428$, indicated however, that the first and second baseline heart rates did not differ significantly.

1. The trend in normalized heart rate plotted at five-second intervals is presented in Figure 1. The solid curve represents the

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Insert Figure 1 about here

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mean normalized heart rate for all subjects who soothed and received a single injection ($n = 52$). The upper and lower curves represent the loci of the upper and lower 95% confidence intervals, respectively. The curve reflects only the mean of the normalized heart rate for the entire group at a specific time. Nevertheless, this curve shows that the injection was associated with an elevated heart rate that began immediately after the injection, and reached a peak approximately 30 to 50 seconds later. Then a gradual return to baseline occurred during the remainder of the three-minute observation period.

2. The mean maximum fractional increase in heart rate for each age group is presented in Table 3. Based on all subjects for whom a

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Insert Table 3 about here

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maximum increase in heart rate was obtained (n = 93), the overall mean maximum fractional increase was 26.31% (SD = 15.26%). There were no statistically significant age or sex differences based on results of a two-way ANOVA. However, a significant Sex by Age interaction, $F(4, 84) = 2.875$, $p<.05$ was found. At 2, 15, and 18 months of age the maximum fractional increase in heart rate was higher for females than for males, but the reverse was true at ages 4 and 6 months.

When mean maximum fractional increases in heart rate for each age group were analyzed by race, the maximum increase was consistently higher at each age for nonwhites, (blacks, Hispanics, and Orientals combined) than for whites. An age by race two-way ANOVA, $F(1, 84) = 5.21$, $p<.05$, confirmed that racial differences were statistically significant.

Subjects who received two injections showed smaller mean maximum fractional increases in heart rate than those who received only one injection. However, t tests, $t(16) = 0.459$ for the 15-month-age group and $t(14) = 0.970$ for the 18-month-age group, indicated that these differences due to number of injections were not significant.

Mean maximum fractional increase in heart rate was also compared between the children in each age group who soothed or did not soothe. Soothing, also referred to as behavioral soothing, was defined as cessation of crying for at least a 10-second interval followed by no return of extended crying within 3 minutes. First, t tests were used to compare the mean maximum fractional increase in heart rate in those

subjects who soothed and received one or two injections. The results, $t(13) = 0.447$ for the 15-month-age group and $t(10) = 0.085$ for the 18-month-age group, were not significant at $p<.05$.

Since subjects did not differ based on number of injections received, the data for one and two injections were combined. These data and the nonsignificant results of t tests at each age for soothed and not soothed subjects are presented in Table 4. A two-way ANOVA on

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Insert Table 4 about here

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age and soothability yielded no significant effects as a function of either soothability (soothed and not soothed groups), $F(1, 84) = 3.63$, or age, $F(4, 84) = 1.03$. However, a one-way ANOVA on soothability was significant, $F(1, 92) = 4.59$, $p<.05$, indicating that soothed infants had smaller increases in heart rate than nonsoothed infants.

The mean maximum fractional increase in heart rate was fitted with a second-order equation, $R^2 = 0.9562$, $F(2, 2) = 21.70$, $p<.05$. Therefore, a significant quadratic relationship existed between mean maximum fractional increase in heart rate and age, such that children in the youngest and oldest age groups had the highest increases in heart rate. However, a one-way ANOVA on age was not significant, $F(4, 89) <1.00$.

3. Time in seconds to reach maximum heart rate for each age group for those receiving a single injection is shown in Table 5.

Insert Table 5 about here

This analysis did not include subjects receiving two injections because if the maximum heart rate occurred after the second injection, the time to maximum heart rate would be prolonged due to the additional time involved in administering the second injection, making comparisons impossible. The mean time to reach maximum heart rate for all subjects (n = 80) was 47.5 seconds (SD = 22.82 seconds). This finding is consistent with the data on normalized heart rate showing that the time to reach maximum increase was between 30 and 50 seconds. Therefore, the maximum heart rate did not correspond with any of the steps of the injection procedure, but rather occurred during the postinjection phase.

To determine the effects of sex and age on time to maximum fractional increase in heart rate, a two-way ANOVA yielded a statistically significant main effect of age, $F(4, 70) = 2.97$, $p<.05$. However, there was no significant effect of sex, $F(1, 70) = 2.62$, or interaction, $F(4, 70) = 1.69$. A similar analysis of race and age produced no statistically significant effects for race, $F(1, 70) = 2.51$; age, $F(4, 70) = 2.11$; or interaction, $F(4, 70) = 0.41$.

The times to maximum heart rate were also compared within each age group for those who soothed or did not soothe. The time to maximum heart rate tended to be faster in the soothed age groups, as may be seen in Table 6. However, only the 6-month group showed a

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Insert Table 6 about here

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significant difference. A one-way ANOVA, $F(1, 78) = 6.91$, $p<.05$, confirmed that soothed infants took significantly less time to reach

maximum heart rate than nonsoothed infants. However, a two-way ANOVA performed on age and soothability yielded no significant effects for age, $F(4, 70) = 1.67$; soothability, $F(1, 70) = 2.35$; or interaction, $F(4, 70) = 0.5$.

When the data in Table 6 were fitted with a linear equation, $R^2 = 0.3935$, $F(1, 3) = 1.95$, $p > .05$, and a second-order equation, $R^2 = 0.8250$, $F(2, 2) = 4.71$, $p > .05$, regression analysis also yielded nonsignificance.

Oxygen saturation. The analysis of oxygen saturation was more limited than for heart rate because of wide variability in the data. Both minimum oxygen saturation (lowest saturation recorded) and time to minimum oxygen saturation (time in seconds until lowest saturation first occurred) were obtained using two different criteria. The liberal criterion used all subjects with oxygen saturation levels below 100%. The conservative criterion used only subjects with saturation levels below 95% (the normal range was considered to be 95% to 100%); consequently, the second method included fewer subjects. The baseline for all subjects was the oxygen saturation value at "in" time, which was below 95% in the case of 12 infants. Means and standard deviations for both methods are presented by age level in Table 7. As the data in Table 7 show, the mean minimum oxygen

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Insert Table 7 about here

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saturation obtained using the conservative method resulted in consistently lower saturation levels than the liberal method.

The liberal method resulted in overall means for minimum oxygen

saturation of 86.68% (*SD* = 13.16%) and for time to minimum oxygen saturation of 43.13 seconds (*SD* = 33.00 seconds). The conservative method resulted in overall means for minimum oxygen saturation of 82.74% (*SD* = 13.70%) and for time to minimum oxygen saturation of 42.98 seconds (*SD* = 34.52 seconds).

To determine if significant differences existed among the age groups, a one-way ANOVA was performed. Since analysis using both methods yielded identical results in terms of significant or nonsignificant effects, only the results for the conservative method are presented. The results were not significant, $F < 1.00$. In addition, regression analysis yielded similar nonsignificant results for both methods.

Unlike the mean minimum oxygen saturation that fell within a narrow range for all the age groups, the mean time of occurrence demonstrated much greater variability with age. To determine if significant age differences existed in time to minimum oxygen saturation, the data were analyzed in the same way as indicated above for minimum oxygen saturation levels. One-way ANOVAs did not yield significant effects for either method, $F(4, 63) = 1.71$ for the conservative method. However, regression analysis did reveal a significant quadratic relationship when mean time to minimum saturation versus age was fitted with a second-order equation, $R^2 = 0.9501$, $F(2, 2) = 19.05$ for the conservative method, indicating that the younger age groups and the oldest age group had the longest time to minimum oxygen saturation.

Cry. Three analyses of cry were performed: (a) Time to initial cry, defined as time to first audible cry, (b) time to soothing, and

(c) proportion of children soothed. Soothing, also referred to as behavioral soothing, was defined as cessation of crying for at least a 10-second interval followed by no return of extended crying within 3 minutes; for analysis, two subjects who did not cry were considered soothed. Of the 102 subjects, 71 soothed and 31 did not soothe.

1. The mean time in seconds to initial cry is presented in Table 8. For children receiving two injections, the time to initial cry was

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Insert Table 8 about here

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based on the first injection. The overall mean time to initial cry for the 72 subjects was 2.14 seconds (*SD* = 1.10 seconds), which corresponded very closely to the step of injecting the vaccine (mean time from "in" to "inject" was 2.0 seconds).

To determine the effects of sex and age on time to initial cry, a two-way ANOVA yielded statistically significant main effects of Age, $F(1, 62) = 7.70$, $p<.05$, and Sex, $F(1, 62) = 3.02$, but not for interaction, $F(4, 62) = 0.72$. A similar analysis of race and age produced a statistically significant effect for Age, $F(4, 62) = 2.64$, $p<.05$, but not for Race or interaction, both $F < 1.00$.

To determine if differences existed in time to initial cry among those who soothed or did not soothe in each age group, *t* tests were performed on all but the two oldest groups where the *ns* were too small. The results, $t(11) = 1.298$ for the 2-month-age group, $t(13) = 1.660$ for the 4-month-age group, and $t(20) = 1.609$ for the 6-month-age group, were uniformly nonsignificant at $p<.05$. This finding was corroborated by a one-way ANOVA between soothed and nonsoothed groups,

$F(1, 70) < 1.00$.

Regression analysis also failed to yield a significant relationship between age and time to initial cry when the data in Table 8 were fitted with a linear equation, $R^2 = .1340$, $F(1,3) = 0.46$, $p>.05$, and a second-order equation, $R^2 = .6596$, $F(2,2) = 1.94$, $p>.05$. However, a tendency may be seen in Table 8 for the youngest and oldest age groups to have the fastest times to initial cry. For this reason, a one-way ANOVA on age was performed and the result, $F(4, 67) = 3.46$, $p<.05$ was significant.

2. The mean soothing time for children ($n = 68$) receiving one or two injections is presented in Table 9. To determine the effects of

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Insert Table 9 about here

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race and sex on soothing time, two-way ANOVAs were performed on sex and age, and on race and age. A statistically significant main effect of Age, $F(4, 59) = 2.59$, $p<.05$, was found. However, no significant effects of Sex or interaction, both $F < 1.00$, were found. In terms of race, a significant main effect for age, $F(4, 59) = 4.06$, $p<.05$ was again found, but not for Race, $F(1, 59)$ 1.00, or interaction, $F(4, 59) = 2.06$.

For children receiving two injections, behavioral soothing was timed from the "in" step of the second injection. The overall mean soothing time for the subjects receiving a single injection ($n = 58$) was 81.65 seconds ($SD = 37.79$ seconds). To determine if the soothing time was influenced by the number of injections, t tests were performed on the data of the 15- and 18-month age groups. The

results, t <1.00 for both groups, were not significant, indicating that soothing time was not affected by number of injections.

To determine if a relationship existed between age and soothing time, the data in Table 9 for the single injection groups were fitted with a linear equation with R^2 = .2068 $F(1,3) = 0.78$, $p>.05$ and a second-order equation R^2 = .2724, $F(2,2) = 0.37$, $p>.05$. In both cases the results of regression analysis yielded nonsignificance. However, a one-way ANOVA, $F(4, 64) = 3.06$, $p<.05$, yielded a significant age effect in terms of soothing time.

3. The number of subjects who soothed or did not soothe and the proportion who soothed are given in Table 10. The proportion of

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Insert Table 10 about here

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children who soothed was fitted with a second-order equation, R^2 = 0.9689, $F(2, 2) = 30.83$, $p<.05$. Thus, a significant quadratic relationship was found between age and proportion of children soothed, such that the youngest and oldest children were less likely to soothe as compared to children in the middle age groups.

A 2 x 2 Chi square test was performed to determine if the number of subjects who soothed differed due to the number of injections received. The result was not significant, $\chi^2(1) = 0.55$, $p>.05$. However, a similar Chi square test, $\chi^2(4) = 9.64$, $p<.05$, confirmed that soothability differed significantly across the 5 age levels.

Facial expression. The proportion of children with facial expressions of physical distress or anger was calculated for two phases of the injection procedure: phase 1 or "before bandaid" (from

"in" to application of the bandaid), and phase 2 or "after bandaid" (the 30 seconds immediately after application of the bandaid). These data are presented in Table 11. Only children receiving single

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Insert Table 11 about here

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injections, not crying before "in" time, and who cried throughout phase 1 (n = 83) or phase 2 (n = 76) were included in this analysis. The proportion of children demonstrating either facial expression 100% of the time (total physical distress or anger) for each phase and the proportion of children demonstrating either facial expression more than 50% but less than 100% of the time (predominantly physical distress or predominantly anger) for each phase was calculated.

The data for total physical distress and total anger expressions before and after bandaid for all age groups are plotted in Figure 2,

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Insert Figure 2 about here

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which shows the relationship between facial expression, phase of the injection procedure, and age. The proportion of subjects with a total physical distress expression decreased with age and elapsed time after the injection, whereas the opposite occurred in children with a total anger expression. In addition, the proportion of children with a total physical distress expression before bandaid was greater than after bandaid. The opposite pattern occurred with the proportion of children with a total anger face; a facial expression of total anger was more likely after bandaid than before, especially in the 15- and

18-month age groups.

The proportion of children with a facial expression of total physical distress declined with age in phase 1, as reflected in a significant linear multiple correlation, R^2 = .9161 and $F(1, 3)$ = 32.74, $p<.05$. The same results were obtained when the analysis was expanded to include proportions of children with either an expression of total or predominant physical distress during phase 1. These combined data were fitted with a two segment curve, where Y = 1.0 for ages below 4.28 months, and $Y = AX^B$ for ages 4.28 months and above. The fitted equation, $Y = 1.3664X^{-0.2204}$, yielded a significant coefficient of multiple correlation, R^2 = .9961, $F(1, 2)$ = 506.58, $p<.01$.

As may be seen in Table 11, the proportion of children that showed physical distress during phase 2 declined sharply with age, and no expressions of total physical distress were found after 15 months of age. A similar analysis of the proportion of children with a facial expression of total physical distress during phase 2, fitted with $Y = AX^B$ equation, also yielded a negative exponent on age (- 1.5208) and a significant multiple correlation, R^2 = .9716, $F(1, 3)$ = 102.79, $p<.01$.

When the analysis included the proportions of children with a facial expression of total or predominant physical distress during phase 2, a significant quadratic effect resulted, R^2 = .9732, $F(2, 2)$ = 36.26, $p<.05$). This finding was inconsistent with the previous ones, which showed a linear relationship between facial expressions and age. However, the relationship was a linear one for the first 4 age groups even in this analysis.

For 10 children ages 18 to 21 months who received two injections,

total facial expressions were compared in phase 1 for both the first and the second injection (see Table 12). For the first injection, the

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Insert Table 12 about here

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same pattern existed as in children ages 18 to 21 months who received a single injection. Approximately 60% of children in both groups had a facial expression of total physical distress and about 30% had a facial expression of total anger throughout all of phase 1. However, a striking difference occurred when the infants received the second injection. Now the pattern of facial expression was reversed with 45.5% of the children having a total anger expression compared to 27.7% having a total physical distress expression. A similar comparison could not be performed for phase 2 because it was not possible to observe the facial expression for 30 seconds after the bandaid was applied following the first injection since the second injection was given immediately after this step.

Relationship Between Physiological and Behavioral Responses to Injection

Analyses were performed on the relationship between cry, heart rate, and oxygen saturation. The relationship between duration of physical distress or anger facial expressions and physiological measures could not be examined because videotaping of facial expression ended 30 seconds after the bandaid was applied. However, since these expressions occurred only during crying, for all children whose behavioral soothing time was less than pulse soothing time (duration of time for heart rate to return to baseline within 3

minutes), facial expression also returned to baseline earlier than heart rate.

A total of 71 children stopped crying before their heart rate returned to baseline; only 1 child (age 6 months) had a behavioral soothing time greater than pulse soothing time. Therefore, virtually all children demonstrated behavioral soothing prior to physiological soothing.

The difference between behavioral and pulse soothing times was calculated for all children (n = 52) whose heart rate returned to baseline. The mean overall difference between behavioral and pulse soothing times was 30.92 seconds (SD = 20.66 seconds).

To determine whether the difference between behavioral and pulse soothing time was related to age, correlational analysis, using both linear, R^2 = .1833, $F(1, 3) = 0.67$, $p>.05$, and second-order, R^2 = 0.2493, $F(2, 2) = 0.33$, $p>.05$, equations was performed. The results indicated that differences between soothing time and pulse soothing time were not significantly related to age.

The relationship between cry and oxygen saturation could only be analyzed for subjects (n = 37) who had data on both time to behavioral soothing and time to oxygen soothing (duration of time for oxygen saturation to return to baseline). Because oxygen desaturations often occurred erratically, in many subjects it was difficult to determine a true time to oxygen soothing. Of the 37 subjects, 21 had a time to oxygen soothing less than time to behavioral soothing and 16 had the opposite pattern. To determine if these patterns were significantly different, a Chi square test was performed; the result, $\chi^2(1) = 0.68$, $p>.05$ was not significant.

The relationship between time to minimum oxygen saturation and time to maximum fractional increase in heart rate was analyzed by calculating the absolute difference between the two times for 76 subjects. For 7 subjects, there was no difference between time to minimum oxygen saturation and time to maximum fractional increase in heart rate; for 43 subjects, time to minimum oxygen saturation was less than time to maximum fractional increase in heart rate; and for 26 subjects the opposite pattern occurred. For 35 (46%) of these subjects, the variations in time to minimum oxygen saturation occurred within +15 or -15 seconds of time to maximum fractional increase in heart rate. The finding that the majority (62%) of subjects demonstrated a minimum oxygen saturation before a maximum fractional increase in heart rate was consistent with the comparison of the overall mean times of 43 seconds for time to minimum oxygen saturation and 47 seconds for time to maximum fractional increase in heart rate.

To determine if the absolute differences between time to minimum oxygen saturation and time to maximum fractional increase in heart rate were related to age, the data were fitted with a second-order equation with a coefficient of multiple correlation $R^2 = 0.9923$, $F(2, 2) = 128.91$, $p<.01$. Therefore, a significant quadratic relationship existed, indicating that the youngest and oldest infants had the greatest absolute differences between time to minimum oxygen saturation and time to maximum fractional increase in heart rate. The findings of significant differences between these measures and age were also corroborated, $F(4, 71) = 7.91$, $p<.001$, by a one-way ANOVA.

Effect of Prior Painful Experiences on Physiological and Behavioral Responses to Injection

To analyze the effect of prior painful experiences on the subjects' responses to the injection, a total pain history score was determined for each child by summing the number of painful events as reported by the parent on the Infant Pain Inventory. No attempt was made to "weight" the painful events for severity since the types of painful events reported were usually mild and similar for most of the children. In those children who had a history of hospitalization (n = 7), it was not possible to determine the number of painful procedures they had experienced during the admission, but it was logical to assume that they had experienced some. Therefore, hospitalization was considered a high pain history event. The scores for nonhospitalized painful events ranged from 3 to 25 with a mean of 7.1. The subjects were classified as having a low pain history if their score fell below the mean and a high pain history if their score fell above the mean or they had been hospitalized.

As the data in Table 13 show, the number of painful experiences increased with age, an expected occurrence because older children have more opportunity to experience painful events. When the data were

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Insert Table 13 about here

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fitted with a linear equation, the coefficient of multiple correlation, R^2 = .8199 and $F(1, 3)$ = 13.36, $p<.05$ also confirmed the significant linear relationship between age and number of pain experiences.

Relationship between pain history and heart rate and cry. To examine the relation of pain history to the variables of maximum fractional increase in heart rate, time to maximum heart rate, time to initial cry, and time to behavioral soothing, a series of one-way ANOVAs was performed on each variable as a function of high and low pain history. All results, $F < 1.00$, were not significant.

Next, a series of two-way ANOVAs was used to analyze maximum fractional increase in heart rate, time to maximum heart rate, and time to initial cry as a function of pain history scores and soothability. These results were also nonsignificant, $F < 1.00$, for the main effect of pain history for all variables.

Relationship between pain history and soothing. To address the question of whether pain history had any effect on the proportion of subjects who soothed, the data were analyzed using dummy variable regression. A plot of the proportion soothed versus mean age for high and low pain history revealed a trend toward a quadratic relationship, with $R^2 = 0.9391$, $F(2, 2) = 15.42$, $p > .05$ for the low pain history group and $R^2 = 0.8412$ $F(2, 2) = 5.30$, $p > .05$ for the high pain history group. The dummy variable assumed the value of zero when a child belonged to the low pain history group and assumed the value of one when a child belonged to the high pain history group. To account for the interaction between pain history and mean age, a cross product term was also added to the quadratic equation.

The calculated values of the dummy variable, the coefficient associated with the intercept = -0.2328 and the coefficient associated with the slope = -0.004693, indicated that the high pain history curve fell below the low pain history curve with a very slight change in the

vertical distance between them.

To determine if the difference between the two curves was significant, *t* tests were used to compare the intercepts and the first-order coefficients of the low pain history and the high pain history curves. The results, $t(3) = 2.25$, $p<.06$ for the intercepts and $t(3) = 0.164$, $p>.05$ for the first-order coefficients, indicated that the trend for children with a high pain history to have a lower tendency to soothe was not significant, although the intercept value barely failed to reach significance.

Relationship between pain history and facial expression. To determine whether pain history had any effect on the type of facial expressions the subjects displayed, analyses were conducted on the children in the 6-, 15-, and 18-month age groups. It was not possible to perform a similar analysis on younger children because almost all of the children 2 to 4 months of age had a facial expression of total or predominant physical distress both before and after application of the bandaid.

The data in Table 14 show the proportion of children with low or high pain history scores who had total or predominant expressions of physical distress or anger during the two phases of before and after applying the bandaid. The analysis included children receiving one

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Insert Table 14 about here

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or two injections. For those children who received two injections, their facial expressions before and after the first injection were used, although the observation period after the bandaid was typically

less than 30 seconds, because the second injection was administered soon after the first one. Facial expressions in response to the second injection were not used because it was already found that the type of facial response was influenced by the initial injection.

The data showed that regardless of pain history the children demonstrated the same pattern of facial expressions found earlier; before bandaid physical distress expressions were more common and after bandaid anger expressions were more common. However, compared to the total number of children (n = 32) with these expressions before the bandaid, after the bandaid fewer children in the low pain history group (n = 23) no longer displayed these expressions than in the high pain history group (n = 30). A Chi square test was performed on the difference in number of children with low (n = 9) and high (n = 2) pain history after the bandaid. The result, $\chi^2(1) = 4.45$, $p<.05$, was significant, indicating that children with low pain history were less likely to display physical distress or anger expressions than children with high pain history.

Table 14 also shows that children with high pain history were more likely than children with low pain history to show physical distress expressions before and anger expressions after the bandaid. To determine if these differences were significant, the proportions were tested the binomial distribution. The obtained z scores of 1.92 for the "before bandaid" data and 0.58 for the "after bandaid" data were not significant, indicating that the facial expressions displayed by the infants did not differ significantly as a function of their pain history scores.

Summary

The mean maximum fractional increase in heart rate was 26.31% (SD = 15.26%); the mean time to maximum fractional increase in heart rate was 47.5 seconds (SD = 22.82 seconds). A significant sex by age interaction indicated that in females 2, 15, and 18 months of age the maximum fractional increase in heart rate was higher than for males, but the reverse was true at ages 4 and 6 months. The maximum increase was consistently higher at each age for nonwhites than for whites. There were no significant sex or race differences for time to maximum heart rate.

Both the maximum fractional increase in heart rate and the time to maximum heart rate were not influenced by the number of injections, but were significantly related to the subjects' tendency to soothe. Soothed infants had smaller increases in their maximum heart rates and shorter times to their peak heart rates than nonsoothed infants.

A significant quadratic relationship existed between mean maximum fractional increase in heart rate and age, such that children in the youngest and oldest age groups had the highest increases in heart rate. However, neither a linear nor a quadratic relationship was found between time to maximum heart rate and age.

When all subjects with oxygen saturation levels below 100% were used, the means for minimum oxygen saturation were 86.68% (SD = 13.16%) and for time to minimum oxygen saturation were 43.13 seconds (SD = 33.00 seconds). When all subjects with levels below 95% were used, the means for minimum oxygen saturation were 82.74% (SD = 13.70%) and for time to minimum oxygen saturation were 42.98 seconds (SD = 34.52 seconds). Nonsignificant differences existed among the age groups for

minimum oxygen saturation. However, a significant quadratic relationship was found between time to minimum saturation and age, indicating that the two youngest age groups and the oldest age group had the longest time to minimum oxygen saturation.

The mean time to initial cry was 2.14 seconds (SD = 1.10 seconds). Males had a significantly shorter time to initial cry than females, although race and soothability were not significantly related to time to initial cry. A nonsignificant trend was found for the youngest and oldest age groups to have the shortest times to initial cry. The mean soothing time for children receiving one injection was 81.65 seconds (SD = 37.79 seconds). Soothing time was not affected by number of injections, sex, or race. No significant relationship was found between age and soothing time. A significant quadratic relationship existed between age and proportion of children soothed, such that the youngest and oldest children were less likely to soothe as compared to those in the middle age groups. The number of subjects who soothed did not differ due to the number of injections received.

Facial expressions of physical distress and anger showed a linear relationship with age and time in all instances except after application of the bandaid in the 18-month age group. The proportion of subjects with physical distress expressions decreased with age while anger expressions increased with age. The proportion of children with physical distress expressions was greater before application of the bandaid, whereas facial expressions of anger were greater after application of the bandaid, especially in the 15- and 18-month age groups. For infants ages 18 to 21 months who received two injections, the pattern of facial expressions before application

of the bandaid was reversed with more children having an anger expression than a physical distress expression.

Seventy of 71 subjects children ceased crying before their heart rate returned to baseline. The mean difference between behavioral and pulse soothing times was 30.92 seconds (SD = 20.66 seconds). The differences between these times were not significantly related to age. The relationship between cry and oxygen saturation was also not significant. However, the differences between time to minimum oxygen saturation and time to maximum fractional increase in heart rate showed a significant quadratic relationship, such that the youngest and oldest infants had the largest differences between these times.

The pain history scores for nonhospitalized painful events ranged from 3 to 25 with a mean of 7.1 and showed a significant linear relationship with age. Pain history was not related to maximum fractional increase in heart rate, time to maximum heart rate, time to initial cry, and time to behavioral soothing. There was a trend for pain history to have an effect on the proportion of subjects who soothed, such that children with a high pain history had a lower tendency to soothe.

In terms of the relationship between pain history and facial expressions children with low pain history were significantly less likely to display physical distress or anger expressions after application of the bandaid than children with high pain history. Although children with high pain history were more likely than those with low pain history to display physical distress expressions before and anger expressions after application of the bandaid, these differences were not significant.

Discussion

The present findings shed further light on differential emotions theory and new information on the effect of infants' prior pain experiences on their present pain responses. The relationship between age and facial expressions were remarkably similar to those reported by Izard (Izard, Hembree, Dougherty, & Spizzirri, 1983; Izard, Hembree, & Huebner, 1987). According to differential emotions theory, the change to anger expressions in response to pain with increasing age represents a higher level of cognitive coping (Izard, 1977). Whether maturation and advanced coping are the reasons for this change in expression is speculative. As Izard cautioned, "Facial expressions provide no direct evidence relating to emotion experience. Statements or implications regarding emotion expressions are inferences from differential emotions theory" (Izard, Hembree, Dougherty, & Spizzirri, 1983).

Several findings from this study suggest that experience also affects facial expression. For example, in the 18- to 21-month-age group receiving one or two injections, the majority of children in both injection groups displayed physical distress expressions immediately after receiving the first injection. However, in the group receiving two injections, more children displayed anger expressions than physical distress expressions immediately after receiving the second injection.

Related evidence comes from two subjects who cried after the first injection and briefly stopped crying before the second injection. In both cases the time to initial cry for the second injection was much shorter than the time to initial cry for the first

injection (1.00 vs 3.06 seconds and 1.89 vs 0.77 seconds). For a third child who did not cry in response to the first injection, the time to initial cry for the second injection (0.4 seconds) was considerably less than the mean of 1.40 seconds for his age group. These results are consistent with those reported by Franck (1986) on newborns receiving two heel lances. Both time to initial movement and cry were shorter in response to the second lance than the first one. Thus, repeated stimulation may provide for short-term learning that hastens the appearance of an anger expression and cry.

The findings in this study also provide important, but preliminary, evidence that longterm learning may also play a role in facial expression and soothability. These results are particularly striking, considering that the two pain history groups were not dramatically different. The fact that subjects with high scores relative to those with low scores displayed significantly more physical distress or anger expressions after application of the bandaid suggests that past pain is not forgotten but continues to exert an influence on present pain responses. To our knowledge this is the first attempt to address this aspect of pain in infants, and provides some basis for questioning those arguments that very young children do not remember or require treatment to relieve pain (Campbell, 1989). Recent research on animals has provided evidence for the effect of learning on neural structure. Using Pavlovian conditioning, researchers trained rabbits to blink each time a bell was rung by pairing the bell with a mild puff of air directed into one eye. The rabbits' brains were then examined for the number of synaptic connections in the areas of the cerebellum that controlled

eyeblink behavior. Significantly more connections were found on the side trained to blink as compared to the contralateral (nonblink) side (Greenough & Anderson, 1991).

Differential emotions theory also proposes that wide individual differences exist in emotion thresholds. Pain activates emotion, and the pain-emotion interactions can increase and prolong the child's negative affective response. Thus, the child's ability to be soothed following pain is assumed to be more a function of individual character than of age (Izard, Hembree, Dougherty, & Spizzirri, 1983). In this study, we found that age, as well as pain history, was significantly related to soothability. No attempt was made to assess the subjects "character," which may have contributed to the variability in the subjects' responses to the injection. Children with low pain histories showed a greater tendency to soothe than children with high pain histories. It is possible that children who have experienced more painful events may become sensitized to pain and show distress for a longer period. Children who have been observed during repeated painful procedures often demonstrate increasing behavioral distress (Katz, Kellermen, & Siegel, 1980; Sandler et al., 1992).

The most parsimonious explanation of these effects, however, would seem to be differences in learning and experience, rather than "character" differences. Thus, while some of our findings support differential emotions theory, others suggest that maturation or character are not the sole determiners of the change in facial expression from physical distress to anger, or in tendency to soothe. Consequently, the theory's unidimensional model was not supported.

The data also did not support the hypotheses that infants with high pain history would demonstrate anticipatory behaviors or heightened and prolonged physiological responses, although the data on behavioral soothing showed a trend toward less soothability in this group. None of the subjects showed evidence of anticipating the injection by crying when seeing the needle or moving their arm or leg or the nurses' hand away to avoid the injection. It was not possible to test the hypothesis concerning the appearance of an anger expression at an earlier age in infants with high pain history as opposed to those with low pain history because anger expressions occurred so infrequently in the younger age group.

The findings also reflect the relative merits of using heart rate, oxygen saturation, cry, and facial expression as simultaneous responses in the assessment of pain. Among the four measures, perhaps the best indicator of acute pain was facial expression, a finding supported by other research (Johnston & Strada, 1986). However, duration of cry seemed to be a better measure of behavioral soothing than facial expression.

Heart rate changes overall were also fairly consistent, with a rise above baseline occurring in virtually all of subjects. However, the change in heart rate among individual children varied greatly, sometimes even falling below baseline, a pattern observed by others (Johnston & Strada, 1986; Owens & Todt, 1984). Heart rate was affected by soothability; maximum heart rate and time to reach maximum were less in children who soothed. Unlike facial expression and cry that were immediately affected by the injection, the time to reach maximum heart rate occurred after the injection procedure was

completed. However, heart rate also took longer than cry or facial expression to return to baseline, indicating that it may be a more specific measurement of physiological soothing.

Changes in oxygen saturation were found to vary greatly with wide ranges in minimum saturations and times to minimum and return to baseline saturations. Unlike the relatively smooth and consistent pattern of changes in heart rate, the decreases in oxygen saturation were typically erratic. Like heart rate, the oxygen saturation reached its lowest point after the injection was completed. Therefore, while measurement of oxygen saturation provided evidence that the infants experienced physiological stress in response to the injection, it did not provide much useful pain assessment information beyond that provided by the other three measures.

In terms of the relationship between physiological and behavioral responses to pain, the findings showed that the behavioral responses of cry and facial expression returned to baseline sooner than the physiological response of heart rate for virtually all subjects. In terms of the relationship between time to minimum oxygen saturation and time to maximum fractional increase in heart rate, the general trend was for the former to occur before the latter. However, changes in oxygen saturations were so erratic that this trend was difficult to identify for most subjects.

If children appear calm or "recovered" before the body's physiological distress has abated, it seems prudent to question if soothing behavior alone is a valid sign of recovery. Gunnar, Fisch, and Malone (1984) found that when unanesthetized newborns were given a pacifier during circumcision, they cried and moved less than a control

group without a pacifier. However, postcircumcision cortisol levels were similarly elevated in both groups. The decreased crying and movement, which made the pacifier group appear less upset, did not accurately reflect the concomitant high level of physiological distress. Animals studies have also shown this dissociation between behavior and cortisol changes (Levine, 1982).

Analyses of the relationship between age and several variables yielded a consistent U-shaped developmental trend. This was the case with maximum fractional increase in heart rate, time to minimum oxygen saturation, absolute difference between time to maximum fractional increase in heart rate and time to minimum oxygen saturation, and proportion of children soothed. Although not statistically significant, a similar trend was found for time to initial cry.

That children in the youngest and oldest age groups were least likely to soothe may be explained by the developmental characteristics of very young infants and toddlers. McGraw (1941) found that during the first month of life infants exhibited an increased intensity of the neuromuscular and crying responses to a pinprick, followed by a diminution of these responses. McGraw attributed this change to the developing inhibitory influence of the cortex upon the neuromuscular activities of subcortical centers.

Brazelton (1962) also found an increase in the duration of routine crying during the first 6 weeks and hypothesized that crying serves the neurophysiological function of discharging accumulated tension. With maturation, improved neuromuscular organization allows the infant to discharge tension in other ways, such as voluntary movement, which decreases the need for crying. Such findings may

reflect a greater perception of pain in very young infants due to immaturity, rather than an insensitivity to pain, as some would argue. Because the descending inhibitory pain pathways are not fully developed (Anand & Carr, 1989), they may be less effective in inhibiting the pain response than in older infants.

In contrast, children in the 18- to 21-month age group may have been exhibiting the psychosocial characteristics of toddlerhood. This stage of development is devoted to mastering autonomy (Erikson, 1963). The significantly greater physiological upset and lower tendency to soothe may reflect this age group's difficulty in coping with the sudden injection pain or the use of their learned social skills, such as crying, to solicit attention and comfort. Therefore, it is unlikely that they perceive greater pain, but rather react longer and more intensely to it.

While the age differences can be explained, the sex and race findings of shorter times to initial cry in males than females and greater increases in heart rate in nonwhite than white subjects, are difficult to interpret. Studies of infant pain have only rarely reported sex effects, and have found either no difference (Owens & Todt, 1984) or isolated ones (Craig, McMahon, Morison, & Zaskow, 1984; Grunau & Craig, 1987; Grunau, Johnston, & Craig, 1990). Ours appears to be the first study to analyze race differences. Whether our findings on sex and race are real or are an artifact of our sample, and whether such differences are clinically relevant cannot be determined at this point.

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Table 1

Demographic Characteristics of Subjects (N=105)

		Gender		Ethnic group			
Age group (mean age) (months)	N	Male	Female	White	Black	Hispanic	Oriental
2 - 3 (2.18)	17	9	8	9	5	2	1
4 - 5 (4.29)	18	9	9	11	5	2	0
6 - 8 (6.78)	27	9	18	21	5	1	0
15 - 17 (15.65)	22	11	11	17	4	1	0
18 - 21 (18.62)	21	11	10	17	1	2	1
Total	105	49	56	75	20	8	2

Table 2

Types of Vaccines Given in Each Age Group

Age group (months)	Single injection	Double injections
2-3[a]	DTP (17)[b]	-
4-5[a]	DTP (17), MMR (1)	-
6-8	DTP 26), MMR (1)	-
15-17	MMR (17)	MMR + DTP (5)
18-21[a]	DTP (5), Hib (1), MMR (3)	Hib + DTP (7), MMR + DTP (5)

Note. Abbreviations are DTP - diphtheria, tetanus, pertussis; MMR - measles, mumps, rubella; Hib - Haemophilus influenzae type B.

[a]These children also received oral polio before DTP vaccine.

[b]Number of subjects in parentheses.

Table 3

Maximum Fractional Increase in Heart Rate - Single vs Double Injections

Single injection				Double injection			
Mean age (mos.)	N	Mean increase	(SD)[a]	Mean age (mos.)	N	Mean increase	(SD)[a]
2.19	16	0.2769	(0.1300)	-	-	-	
4.25	16	0.2432	(0.1342)	-	-	-	
6.78	27	0.2341	(0.1452)	-	-	-	
15.64	14	0.2626	(0.1267)	15.75	4	0.2283	(0.1162)
18.86	7	0.4012	(0.2438)	18.33	9	0.2895	(0.1871)

[a]Standard deviation.

Table 4

Maximum Fractional Increase in Heart Rate Among Subjects Who Soothed or Did Not Soothe

Soothed				Not soothed				t test[a]
Mean age (mos.)	N	Mean increase	(SD)[b]	Mean age (mos.)	N	Mean increase	(SD)[b]	
2.12	8	0.2477	(0.0582)	2.25	8	0.3061	(0.1757)	0.834 (df,14)
4.22	9	0.2062	(0.1329)	4.28	7	0.2908	(0.1616)	1.191 (df,14)
6.77	22	0.2164	(0.1533)	6.80	5	0.2822	(0.1401)	0.847 (df,25)
15.53	15	0.2531	(0.1175)	16.33	3	0.2647	(0.1718)	0.135 (df,18)
18.58	12	0.2625	(0.1892)	18.60	5	0.4143	(0.2839)	1.211 (df,15)

[a]Not significant at $p<.05$.

[b]Standard deviation.

Table 5

Time to Maximum Heart Rate

(Single Injection)

Mean age (months)	N	Mean time (SD)[a] (seconds)	
2.18	16	64.15	(30.47)
4.25	16	49.35	(17.32)
6.78	27	39.71	(17.99)
16.86	14	44.15	(13.66)
18.86	7	42.59	(29.99)

[a]Standard deviation.

Table 6

Time to Maximum Fractional Increase in Heart Rate Among Subjects Who Soothed or Did Not Soothe

Soothed				Not soothed				t test[a]
Mean age (mos.)	N	Mean increase (seconds)	(SD)[b]	Mean age (mos.)	N	Mean increase (seconds)	(SD)[b]	
2.12	8	55.40	(21.48)	2.25	8	72.90	(36.78)	1.087 (df, 14)
4.12	9	49.29	(15.60)	4.29	7	49.43	(20.63)	0.015 (df,14)
6.77	22	36.30	(16.51)	6.80	5	54.70	(18.11)	2.125 (df,25)
15.45	11	44.36	(13.51)	16.33	3	43.35	(17.30)	0.100 (df,12)
18.80	5	39.52	(32.03)	19.00	2	50.25	(33.59)	0.334 (df,5)

[a]Not significant at $p<.05$, except for 6-month age group.

[b]Standard deviation.

Table 7

Minimum Oxygen (O_2) Saturation and Time of Occurrence

Age (months)	Minimum O_2 saturation (%) N	Mean (SD)[a]	Time (seconds) N	Mean (SD)[a]
		Conservative Method[b]		
2	14	81.28 (14.14)	14	58.85 (47.56)
4	12	85.75 (9.76)	12	51.26 (41.90)
6	18	82.94 (11.61)	18	32.67 (20.29)
15	9	80.78 (20.98)	9	30.13 (13.75)
18	12	82.58 (14.35)	11	41.14 (31.70)
		Liberal Method[c]		
2	16	83.00 (14.24)	16	61.15 (47.30)
4	15	88.00 (9.85)	15	50.40 (37.63)
6	26	87.27 (11.65)	26	35.65 (24.77)
15	17	88.18 (16.91)	17	33.75 (18.30)
18	17	86.59 (13.52)	16	40.39 (30.32)

[a]Standard deviation.

[b]Subjects with a decline in oxygen saturation below 95%.

[c]Subjects with a decline in oxygen saturation below 100%.

Table 8

Time to Initial Cry

Mean age (months)	N	Mean time (seconds)	(SD)[a]
2.15	13	1.70	(0.96)
4.33	15	2.75	(1.20)
6.73	22	2.25	(1.10)
15.73	11	2.34	(0.85)
18.73	11	1.40	(0.88)

[a]Standard deviation.

Table 9

Soothing Time - Single vs Double Injections

Single injection				Double injection			
Mean age (mos.)	N	Mean time (seconds)	(SD)[a]	Mean age (mos.)	N	Mean time (seconds)	(SD)[a]
2.12	8	93.59	(23.97)	-	-	-	
4.30	10	59.15	(26.03)	-	-	-	
6.76	21	94.24	(38.37)	-	-	-	
15.50	12	79.77	(79.77)	15.75	4	81.28	(36.30)
18.71	7	58.24	(33.31)	18.43	7	67.43	(32.52)

[a]Standard deviation.

Table 10

Number of Subjects Who Soothed or Did Not Soothe and Proportion Soothed

Mean age (mos.)	Number soothed	Number not soothed	Proportion soothed
2.18	8	9	.4706
4.29	10	7	.5882
6.78	22	5	.8148
15.65	17	3	.8500
18.62	14	7	.6667

Table 11

Facial Expressions Before and After Bandaid

Mean age (months)	N	Total Physical Distress [a]	Total Anger [a]	Predominant Physical Distress[b]	Predominant Anger[b]
			Before bandaid[c]		
2.18	17	0.9412	0.0	0.0588	0.0000
4.28	17	0.8889	0.0	0.1111	0.0000
6.77	26	0.8461	0.1154	0.0385	0.0000
15.62	16	0.7500	0.2500	0.0000	0.0000
18.86	7	0.5714	0.2857	0.1429	0.0000
			After bandaid[d]		
2.19	16	0.6250	0.1250	0.1875	0.0625
4.25	16	0.1875	0.1875	0.5000	0.1250
6.80	25	0.1600	0.1200	0.2000	0.5200
15.77	13	0.0000	0.6154	0.1538	0.2308
1917	6	0.0000	0.6667	0.3333	0.0000

[a]Proportion of subjects displaying facial expression 100% of time.

[b]Proportion of subjects displaying facial expression more than 50% but less than 100% of time.

[c]Before: From "in" time to application of bandaid.

[d]After: 30-second interval after application of bandaid.

Table 12

Facial Expressions Before Bandaid[a]

(Two Injections)

Mean age (mos.)	N	Total physical distress[b]		Total anger[b]	
		#1[c]	#2[c]	#1	#2
18.5	10	0.6	0.2727	0.3	0.4545

[a]From "in" time to application of bandaid.

[b]Proportion of subjects displaying facial expression 100% of time.

[c]First injection.

[d]Second injection.

Table 13

Pain History Scores

Mean age (months)	N	Mean score	(SD)[a]	Range
2.18	17	5.53	(1.84)	3 - 9
4.08	12	5.92	(1.73)	4 - 9
6.77	22	7.09	(2.26)	3 - 11
15.63	19	8.47	(5.35)	3 - 25
18.59	17	7.76	(3.05)	3 - 14

[a]Standard deviation.

Table 14

Facial Expressions Before and After Bandaid in Relation to Low and High Pain History

Pain history score	N	Physical Distress[a]	Anger[a]
		Before Bandaid[b]	
Low	32	.71875	.28125
High	32	.90625	.09375
		After Bandaid[c]	
Low	23	.30435	.69565
High	30	.23333	.76666

[a]Proportion of subjects demonstrating facial expression between 50% to 100% of time.

[b]From "in" step to application of bandaid.

[c]30-second interval after application of bandaid.

Figure Captions

Figure 1. Normalized Heart Rate vs Time for All Subjects Who Soothed (N = 52)

Figure 2. Proportion of Subjects' with Total Physical Distress and Total Anger Expressions Before and After Bandaid (Single Injection) vs Age

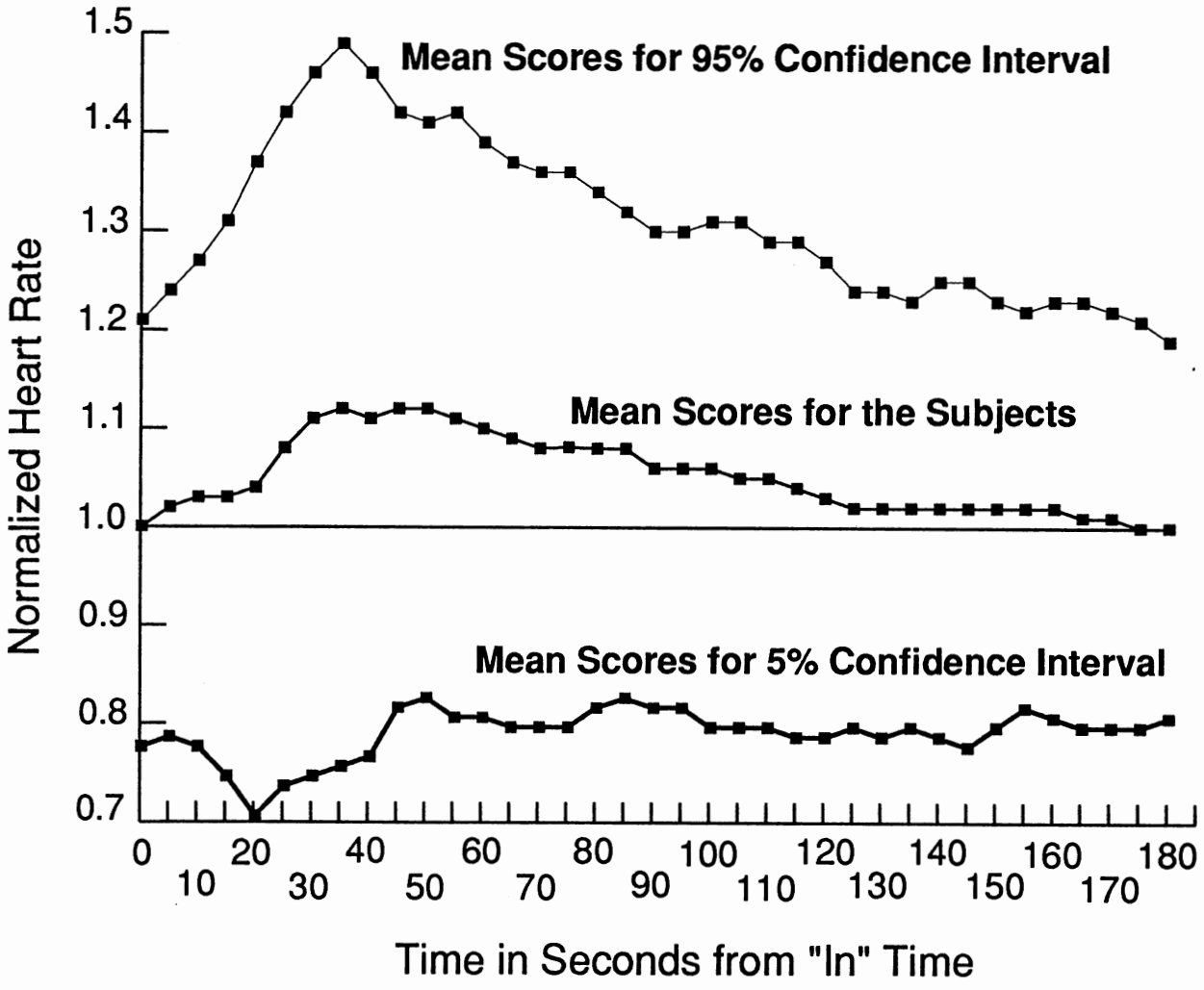

Figure 1. Normalized Heart Rate vs Time for Subjects Who Soothed (N = 52)

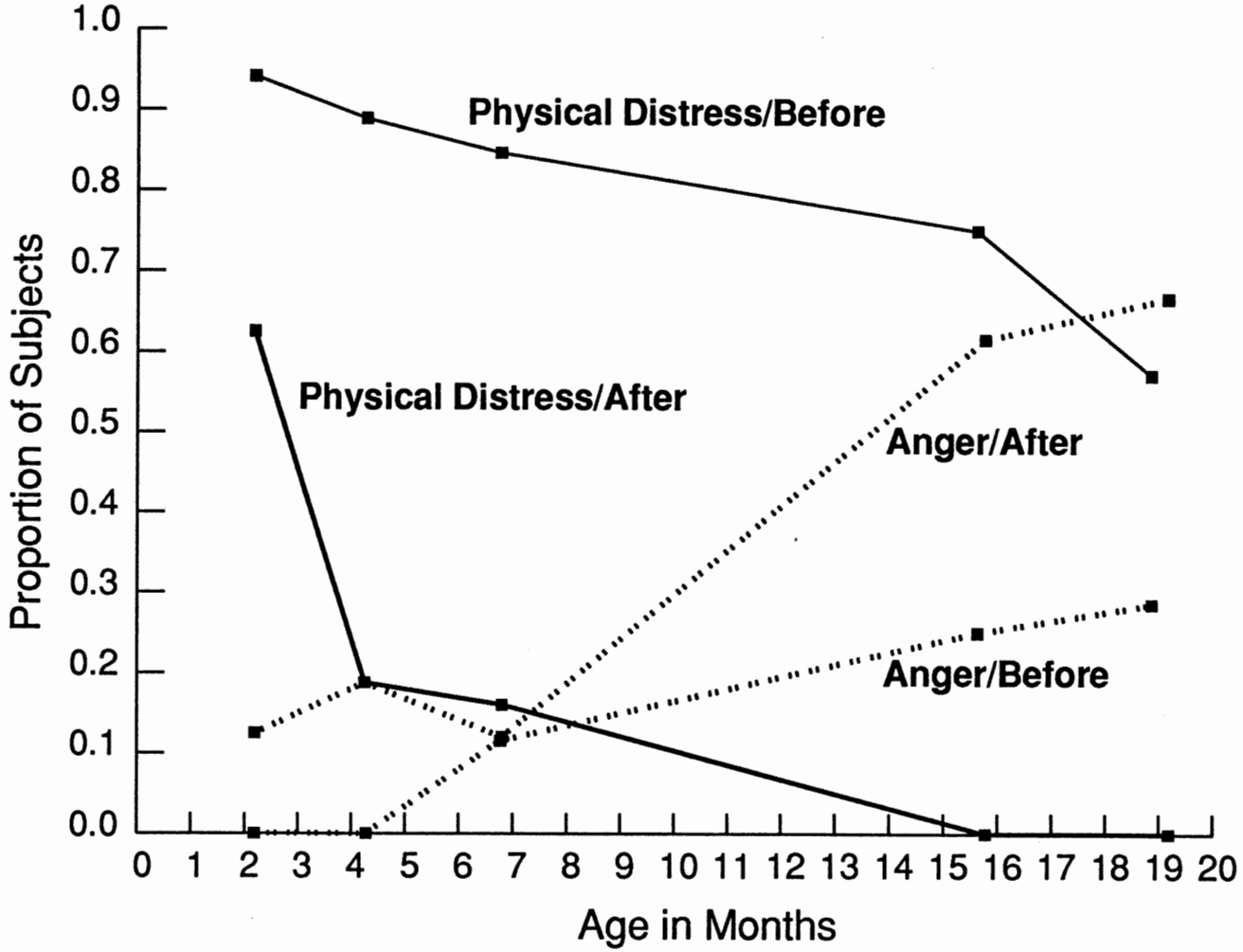

Figure 2. Proportion of Subjects with Total Physical Distress and Total Anger Expressions Before and After Bandaid (Single Injection) vs Age

APPENDIXES

APPENDIX A

REVIEW OF LITERATURE

INFANT PAIN: A REVIEW OF THE LITERATURE

Although pain is a universal sensation experienced by all humans, beliefs about pain have changed dramatically over the past 2,000 years. Past and present hypotheses about pain that influence current pain control practices are pain as punishment, pain as a warning, pain as emotion, pain as a neurotransmission, pain as a challenge to science, and pain as a complex reaction (Donovan, 1989).

Evolving knowledge about pain is changing our understanding of the neurophysiological basis for pain and its assessment and management. Most of these changes have focused on pain in adults, with children, especially infants, following slowly behind in benefitting from these advances. Therefore, the need for additional research on pediatric pain as addressed in the present study is critical to the ultimate goal of relieving pain.

The following review of literature presents a historical overview of beliefs about infant pain, the physiology of pain and pain mechanisms in very young children, evidence for pain in infants, research on infant's memory of painful events, potential benefits of pain control, and a summary of how the present state of knowledge about infant pain relates to the present study's research questions. The research discussed under "General Background" comes from literature primarily published during the last one and a half centuries, whereas the studies reviewed under "The Study of Pain in Infants" are much more current since the majority of research has been done in the last ten years. Although the present study is concerned with pain in infants ages 2 to 21 months, the review includes

considerable research directed at the pain responses of newborns. Perinatal pain research has dominated the field of infant pain, especially in terms of physiological responses.

General Background

As a prelude to the extensive discussion of our current understanding of the present state of infant pain, a brief overview of traditional definitions of pain, past beliefs about infants' ability to feel pain, competing theories of pain transmission, and current knowledge of pain physiology is presented.

Definitions of Pain

Despite the universality of pain as a human experience, a succinct definition of pain as a condition with physiological, pathophysiological, psychological, emotional, and affective dimensions has only emerged recently. In 1986, the International Association for the Study of Pain adopted the following definition: "Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Pain is always a subjective experience." A note added to the definition stated: "Each individual learns the application of the word through experiences related to injury in early life" (Mersky, 1986). Three aspects of this definition relate directly to pain in infants and to the research questions addressed in the present study. First, pain encompasses both physical and emotional components. Second, pain is a

subjective experience that must be inferred, rather than directly observed or measured. Third, the early experience of pain influences a person's perception of pain.

Since pain is subjective, only the person experiencing pain knows it exists and can describe its characteristics. In the operational definition adopted by the World Health Organization, this aspect of pain is emphasized: "Pain is whatever the experiencing person says it is, existing whenever he says it does" (McCaffery and Beebe, 1989).

Unfortunately, both definitions are of little value with infants who cannot describe their distress, and no definition could be found that specifically addressed that pain can also be communicated through nonverbal means. Logically, a definition of infant pain can be proposed based on inferences from adults' responses to pain: "Pain exists in infants if their physiological and behavioral responses correspond to those of adults exposed to the same noxious stimuli."

Historical Overview of Beliefs about Infant Pain

Before the use of anesthesia in the mid 1800's, adults and children suffered excruciating pain during surgical procedures. When ether and chloroform were introduced to produce deep anesthesia, many opponents considered this practice dangerous, because they believed that pain was necessary for healing and survival. Some authorities believed that anesthesia was akin to death (Pernick, 1985). Initially, children were considered excellent candidates for anesthesia, because of their high sensitivity to pain, difficulty in controlling behavior, and the ease of anesthetization. In fact,

manageability was a key factor in deciding which patients should receive anesthesia; for children (too little to be restrained by reason, yet too big to be restrained easily by force) anesthesia was considered especially useful.

However, some surgeons interpreted the ease of anesthetizing children as a danger, especially in infants. In 1848, Dr. Henry J. Bigelow stated the following in a special report published by the American Medical Association, "The fact that it [young infant] has neither the anticipation nor rememberance of suffering, however severe, seems to render this stage of narcotism [full anesthesia] unnecessary" (Pernick, 1985). Many practicing surgeons began to adopt this philosophy regarding infant pain.

Together with a lack of understanding about pain transmission and the effects of pain on infants, relief of pain became an infrequent practice in regard to very young children. For example, more than 100 years later Henry Barnett, author of a classic pediatric medical textbook wrote, "In early infancy, particularly within the first 3 to 4 months, it is often possible to perform an abdominal operation....under the combined influence of morphine, sugar pacifiers, and local anesthesia" (Barnett, 1972). However, Barnett qualified this use of "light anesthesia" by stating that the success of this practice depends on the "feebleness of the patient." He commented, "Robust infants and children up to school age or beyond usually require a general anesthetic when any is called for." One review of major pediatric medical textbooks published between 1978 and 1985 found that of the cumulative 15,472 pages, only three-and-a-half pages were devoted to pain in children (Rana, 1987).

In addition, Barnett's endorsement of the use of a "sugar pacifier" during surgery has its current proponents. Blass and Hoffmeyer (1991) reported their findings on the use of pacifiers dipped in sucrose to induce analgesia during circumcision. They found that infants given water-dipped pacifiers during the surgical procedure spent less time crying than a control group without pacifiers, and that the effect was further enhanced with a 24% sucrose solution. Despite the limitations of this study (see discussion of Behavioral Evidence of Pain in Infants), other authorities have expressed support for the sugar pacifier. Shoen and Fischell (1991), in reviewing alternative methods of pain relief in neonatal circumcision, suggested that "the noninvasive, risk-free nature of a sucrose-flavored pacifier, deserves wide spread evaluation of its effectiveness."

Probably the greatest evidence regarding lack of attention to pain relief in infants is the observation of clinical practice in hospitals. Anand and Aynsley-Green (1985) found that 76% of the published studies of preterm neonates undergoing thoracotomy for ligation of a patent ductus arteriosus received only "light anesthesia" (nitrous oxide, oxygen, and curare). These infants were totally paralyzed but fully sensate during the surgery. In addition, circumcision is typically performed on newborn males without the benefit of any analgesic or anesthetic agent. In neonatal and pediatric intensive care units numerous procedures, such as insertion of chest tubes, central and peripheral arterial and venous punctures, multiple heel punctures, paracentesis, and lumbar punctures, are routinely performed on infants without pain reducers (Franck, 1987;

Bauchner, May, & Coates, 1992). Such practices would be considered inhumane and barbaric if performed on adults. Ironically, safeguards exist to protect laboratory animals, not human infants, from unnecessary pain. The Council on Scientific Affairs of the American Medical Association (1991) states, "All educational experiences involving animals should be carried out in a humane manner that minimizes pain and uses anesthetic and analgesic drugs when procedures may cause more than momentary or slight pain."

Reasons for lack of pain control in infants are numerous. For example, Stang (1991) asks the question, "Why are physicians so slow to change and adapt to using local anesthesia for circumcisions?" He suggests possible reasons: (1) physicians weren't trained to use local anesthesia for circumcisions; (2) the procedure adds some additional time; (3) physicians are not convinced (despite the overwhelming literature) that local anesthesia really decreases pain; (4) concerns exist about the short-term and long-term complications of the dorsal penile nerve block procedure; and (5) a small minority hope that infant pain will discourage parents from consenting to a circumcision.

All of these reasons are probably accurate, but two reasons appear to permeate beliefs about pain in infants. The first is that health professionals are not convinced pain in infants really exists, and second, many believe that pain reducers carry a much greater risk than lack of their use. Historically, pain was thought to be transmitted along myelinated pain fibers. Since a newborn's spinal cord is not fully myelinated, the logical explanation was that pain was unable to be transmitted along these fibers to the brain. The classic study by McGraw (1941) seemed to provide convincing evidence

of this hypothesis, since the findings appeared to show a developmental trend in young children's response to a painful stimulus. Unfortunately, her study had several weaknesses and the findings pertaining to newborns have been disproven (see discussion under Behavioral Evidence of Pain in Infants). Indeed, current physiological evidence clearly demonstrates that pain is transmitted along unmyelinated C-fibers and that newborns have fully functional pain perception mechanisms (see discussion of Pain Mechanisms in Infants).

Despite the scientific evidence, many health professionals continue to believe that neonates do not feel pain. In a survey of 60 members of the Association of Paediatric Anaesthetists in the United Kingdom, 7% stated that neonates under 1 week are unable to perceive pain; 8% answered that they did not know (Purcell-Jones, Dormon, & Sumner, 1988). In another survey of 112 pediatricians, family practitioners, and surgeons in the United States, beliefs about children's pain were significantly influenced by the child's age. Twenty per cent of surgeons believed that newborns experience pain similar to adults. However, only slightly more than 50% thought that children 2 years of age felt adult pain. Somewhat less than 40% of family practitioners stated that neonates experience pain as adults do. For children 2 years old, the percentage increased to more than 70%. Pediatricians were most liberal; almost 60% believed that newborns and more than 80% believed that youngsters two years of age could feel adult pain (Schechter & Allen, 1986). When 76 nurses practicing in neonatal intensive care units throughout the United States were asked about infants' feeling pain exactly as adults do,

only 35 responded positively. However, 60 of them believed that neonates' pain was undertreated (Franck, 1987).

Even those professionals who believe infants perceive pain continue to withhold analgesics and anesthetics, believing them to be unsafe. For example, in the Purcell-Jones, Dormon, & Sumner study, 53% of the anesthesiologists either usually or always prescribed opioids after major surgery for infants 3 to 12 months of age. The percentage fell to 21% when surgery was considered minor, and the percentage was far less for both types of surgery for children under 3 months of age. In the Schechter and Allen study similar discrepancies between beliefs and practices were found. For example, in response to the question, "At what age do you consider using narcotic analgesics in a child who is subjected to an experience for which you would use them in an adult?" slightly more than 10% of pediatricians and family practitioners stated at birth, and all of the surgeons withheld narcotic analgesics until after 1 month of age. For children up to 2 years, the percentages were similar to those reported above for infants' ability to feel pain similar to adults. Ironically, the physician groups tended to be more liberal in their management of pain in areas in which they were not in direct control. For example, pediatricians were more likely than surgeons to report that analgesics should be used for postoperative pain, but surgeons were more likely than the other two groups to report that analgesics should be used for lumbar punctures.

The reasons for this discrepancy are not known. However, Hoffman's (1975) theory of cognitive dissonance may offer an explanation. Hoffman found that when people cannot aid a victim in

need, the bystanders engage in cognitive restructuring of the situation to justify inaction. In regard to suffering, if nothing can be done to relieve pain, it becomes very uncomfortable to believe that pain is being inflicted on helpless children. Therefore, physicians (and other health professionals) who perform painful procedures choose to believe that the child victim is insensitive to pain to avoid personal discomfort.

Another notable example of the continuing contention that pain relief is dangerous to infants is the American Academy of Pediatrics, Task Force on Circumcision Report (1989) which states that although circumcision is painful, the use of local anesthesia has its own inherent risks, and that reports of extensive experience or follow-up with the technique in newborns are lacking. This influential statement has prompted many practitioners to avoid using a local nerve block, despite numerous studies attesting to its safety. Ironically, in another statement by the American Academy of Pediatrics (1987) its report stated that local or systemic pharmacologic agents are available that permit relatively safe administration of anesthesia or analgesia to neonates having surgical procedures. They further state that such administration is indicated according to the usual guidelines for the administration of analgesia to any high-risk potentially unstable patient and that the decision to withhold such medication should be based on the same medical criteria used for older patients. In fact, the infant's age or perceived degree of cortical maturity should not be reasons for using or not using anesthesia. One can only speculate that the contradictions between these two statements is based on personal biases, not scientific facts.

This brief historical overview demonstrates deeply entrenched beliefs about pain in infants and slow movements towards change. However, research on pain assessment in infants and potential beneficial outcomes from adequate pain control are mounting. As one author has stated, "The burden of proof must now fall on those who believe that neonates do not feel pain . . . If we accept the premise that neonates do feel pain, it is surely inhuman to deny them analgesia. We do not do so to adults, and might be prosecuted if we did so to animals" (Gauntlett, 1987).

Theories of Pain Mechanisms

Several theories have been proposed to explain the phenomenon of pain. Before the nineteenth century two theories had dominated people's beliefs about pain. In ancient Greece (about 300 B.C.), Aristotle believed that pain was felt in the heart as a quality or passion of the soul, a state of feeling that was opposite to pleasure and the epitome of unpleasantness. The function of the brain was to produce cool secretions to reduce the excess heat in the blood around the heart that was produced by pain. He also felt that pain was motivational force as a consequence of immorality or imperfection, a concept that still permeates current thinking about pain as punishment. See Bonica (1990) for a review of Aristotle's position.

By the seventeenth century, considerable evidence had accumulated regarding the role of the brain in sensation. Descartes (1664) described the results of his extensive anatomic studies and believed that sensory stimuli, such as pain, were directly transmitted to the

brain by fine threads that formed the marrow of nerves. Descartes's concept was the precursor of specificity theory that was introduced two centuries later.

The nineteenth century saw the emergence of two opposing theories: the specificity theory and the intensive theory. The specificity (sensory) theory maintained that, just as other sensations have unique receptors, so there exists special pain receptors that respond only to high intensity stimuli. Just like Descartes's theory, it implied a direct connection from the receptor to a brain center where pain was perceived (Schiff, 1858). While this theory has received much support from neurophysiological research that demonstrates the existence of nociceptors, its major weakness is its failure to explain clinical phenomena. It is well known that pain states occur when no direct stimulus exists. Examples include neuralgia (pain produced by previously existing conditions), causalgia (a severe burning pain due to injury of a peripheral nerve), and phantom limb pain (pain sensations in the area of the amputated limb). Also the perception of pain is much more complex than specificity theory implies. Numerous factors can influence pain perception, such as psychologic input (i.e., distraction, stress, relaxation, or imagery) and physical input (i.e., heat, cold, vibration, or pressure).

The intensive (summation) theory proposed that the nerve impulse pattern for pain was produced by intense stimulation of nonspecific receptors. The critical determinants of this theory were stimulus intensity and central summation. Stimulus intensity was the assumption that all fiber endings except those that innervate hair

cells were alike and that the pattern for pain was produced by intense stimulation of nonspecific receptors. The other concept, central summation, did not focus on intense peripheral stimulation to produce pain, but on central processes that influenced pain perception. The basic theory of central summation proposed the existence of a rapidly conducting fiber system which inhibited synaptic transmission in a more slowly conducting system that carried the signal for pain. The specialized input-controlling system normally prevented summation from occurring, thus inhibiting pain. Damage to this system led to pathologic pain states (Goldscheider, 1894).

The strength of the intensive theory is that the concept of central summation and input control explains many of the clinical phenomena of pain. Its major weakness is that it discounts the existing evidence for the existence of specific pain receptors.

In 1965 Melzack and Wall proposed a third theory, the gate control theory, which laid the groundwork for subsequent intense research and current thinking about pain. Their theory challenged the specificity theory and elaborated upon the intensive theory. They sought to combine the concepts of physiological specialization with those of central summation in order to explain the mechanisms by which certain cutaneous stimuli and emotional states alter the level of pain perception, as noted in clinical situations. The three assumptions of the gate control theory were (Melzack & Wall, 1965):

1. the substantia gelatinosa functions as a gate control system that modulates the sensory input before it reaches the T-cells (defined as the first central transmission cells in the dorsal horn, the dorsal gray matter of the spinal cord);

2. afferent patterns in the dorsal column system (the ascending pathway that mediates tactile sensation and proprioception to the medulla) act as a central control trigger which activates selective brain processes that influence the modulating properties of the gate control system;

3. the T-cells activate neural mechanisms that comprise the action system responsible for response and perception.

Melzack and Wall postulated that pain stimulus is influenced by certain features of the input to the spinal cord. These include (1) the activity preceding the stimulus, (2) the stimulus-evoked activity, and (3) the balance of activity between small (pain) fibers and large fibers, specifically, A-beta fibers which mediate pressure. They proposed that pain fibers are constantly active, firing at a spontaneous rate, which keeps the gate open. Once a stimulus is applied, the large and small fibers are activated, but the activation is greater in the large fibers, which partially closes the presynaptic gate and inhibits firing of the T cells. They theorized that the inhibitory effect of pressure fibers on pain fibers is not direct, but mediated by a group of interneurons in the substantia gelatinosa.

Melzack and Wall also proposed that a central control trigger exists that activates particular brain processes to exert control over sensory input. Such a control system could account for the modulating effect of attention, emotion, and memories of prior experience on the perception of pain. They suggested that either of two systems could fulfill such a function: the dorsal column-medial lemniscus system or the dorso-lateral system. Such systems could carry information about the nature and location of the stimulus and conduct so rapidly as to

send messages to the cortex and back to the substantia gelatinosa to effect the gating mechanism.

They finally suggested that once the firing-level of T cells exceeds a critical preset level, a sequence of responses by the action system is initiated. The authors doubted that any isolated area of the brain could be considered the "pain center" since the sequence of activities that occur when the body sustains damage is complex and diverse, involving numerous areas of the brain. Consequently, the action system is not a discrete anatomic site but a complex of pathways, that may project to certain somatosensory areas, the thalamic reticular formation, and the limbic system.

Since Melzack and Wall first proposed their theory, subsequent neurophysiological research has not supported all of their hypotheses. Research has shown that all somatosensory fibers are quiet at rest, rather than spontaneously firing. The substantia gelatinosa interneurons predicted by the authors have not been found. The descending inhibitory systems are still under investigation, but one of those proposed by Melzack and Wall, the spinocervical system, does not appear to exist in man, although it is present in many laboratory animals (Hoffert, 1986).

While the theory of a gate control for pain transmission and perception has not been completely supported, it would be unfair to minimize its contribution to the understanding of pain. Since the publication of Melzack and Wall's classic paper, a great deal of research has been directed at explaining the clinical idiosyncrasies of pain. Such research has continued to support the concept of neuromodulation of pain and has provided scientific evidence for

nonpharmacologic interventions such as cutaneous stimulation, relaxation, and distraction. Previously, such interventions were thought to be more folklore than fact. Melzack and Wall continue to modify their original proposal to take into account emerging neurophysiological research.

Overview of Pain Physiology

Although the neurophysiology of pain is extremely complex and not completely elucidated, pain transmission can be organized into several elements: receptors, tracts to the brain, centers in the brain, descending control systems, and chemical neuromediators. The following is a brief overview of the major physiologic components required for pain transmission.

Pain receptors consist of specialized structures and bare nerve endings that terminate in the skin, internal organs, muscles, and tissue surrounding the bones (Schneider & Tarshis, 1986). Since pain receptors respond selectively to damaging stimuli, they are called nociceptors (from the Latin nocere, to injure) (Martin & Jessell, 1991). The three main types of nociceptors are:

1. mechanical nociceptors that are activated only by strong mechanical stimulation and most effectively by sharp objects;

2. thermal nociceptors that respond when the area is heated to temperatures greater than 45 degrees C;

3. polymodal nociceptors that are activated by mechanical, thermal, and chemical stimuli.

Nociceptors are found at the end of A-delta fibers and C fibers,

which are both primary afferent sensory neurons. However, not all A-delta and C fibers are pain fibers, since some are mechano-thermo receptors. Those that are pain receptors have special attributes: they have very high thresholds to mechanical or thermal stimuli, have small receptive fields, and manifest persistent discharges following removal of the stimuli. Pain fibers are also associated with different types of pain. The small myelinated A-delta fibers are associated with fast pain--a sharp, pricking, and abrupt sensation. The unmyelinated C fibers are associated with slow pain--a longer lasting burning sensation (Melzack & Wall, 1988).

A-delta and C fibers enter the spinal cord in the dorsal horn, a highly complex anatomic and neurophysiological structure that refers to the dorsal gray matter of the spinal cord. The dorsal horn consists of 6 layers of neural cells called laminae. A-delta and C fibers terminate primarily in lamina I (the outermost layer) and lamina V, but also in laminae II and III (an important area known as the substantia gelatinosa). In the laminae the A-delta and C fibers form synapses with neurons whose axons cross the cord and ascend to the brain in several tracts. These tracts are collectively known as the anterolateral system because the pathways ascend in the anterolateral portion of the spinal column (Melzack & Wall, 1988).

The anterolateral system consists of the pathways distinguished by their sites of termination: neospinothalamic, paleospinothalamic, and spinotectal tracts. The neospinothalamic tract (named for its more recent phylogenetic development) runs continuously from lamina I to the ventroposterolateral and posterior thalamus, where it synapses with central neurons that travel to the somatosensory cortex. This

tract mediates fast pain, relayed from the periphery to the spinal cord by A-delta fibers (Martin & Jessell, 1991). It is also proposed that this tract also provides discriminative information about pain (Bonica, 1990).

The paleospinothalamic tract (phylogenetically older; also called spinoreticular tract) arises from laminae I and V and terminates in the reticular formation in the brainstem, medulla, lateral pons, in the hypothalamus, and to the limbic forebrain structures. This tract is important in slow pain mediated by C fibers. The spinotectal tract or spinomesencephalic tract terminates in the tectum of the midbrain, an area that is particularly painful when electrically stimulated (Jessell & Kelly, 1991).

Spinal pain projections to the brain are widespread, but involve three general areas: (1) the reticular formation (a network of neurons running through the core of the brainstem from the medulla to the thalamus), (2) the limbic system (a group of brain areas around the brainstem, including the hippocampus, fornix, cingulate gyrus, and parahippocampal gyrus), and (3) the thalamus. Presumably, each is involved in coding a different aspect of pain. The reticular formation accounts for arousal, the limbic system accounts for emotion, and the thalamus is involved in the actual sensations of pain and integrates information from the other two areas (Schneider & Tarshis, 1986).

The cortex is involved in the neural pain circuit although its exact function is under investigation. For example, damage to many regions of the brain can result in increases in the firing rate of neurons and the perception of pain. In humans, stimulating electrodes

used therapeutically in the periventricular gray region, parts of the thalamus, or the internal capsule reduce the severity of pain, while not affecting tactile sensibility (Jessell & Kelly, 1991).

Evidence strongly suggests that pain transmission is subject to modulation or alteration at descending control regions. Two of these regions appear to be the periaqueductal gray, an area in the midbrain that surrounds the cerebral aqueduct, and the nucleus raphe magnus, the nucleus in the raphe's system that is located in the medulla. When stimulated, both of these systems suppress pain (Schneider & Tarshis, 1986). From the nucleus raphe magnus, fibers descend through the dorsolateral column of the spinal cord to end in the substantia gelatinosa (laminae II and III of the dorsal horn) (Jessell & Kelly, 1991). The interneurons in the substantia gelatinosa form synapses with the pain fibers (A-delta and C fibers) and inhibit their firing.

Neuromediators are biochemicals that have important functions in terms of pain transmission, inhibition, and modulation. Some meuromediators are either excitatory or inhibitory and are responsible for the transmission of impulses across the synaptic cleft. Other chemicals modify neuronal activity.

Once nociceptors are excited by mechanical, thermal, or chemical stimuli in sufficient quantities, biochemical neurotransmitters that activate or sensitize the noxious response are released. These neurotransmitters include potassium, substance P, bradykinin, prostaglandin, and other chemical substances. Potassium is released when cells are damaged. Substance P, an excitatory peptide, is released from unmyelinated nociceptors and causes vasodilation and edema. Bradykinin is released from plasma that is leaking from

surrounding blood vessels. Prostaglandins are generated from the breakdown of phospholipids that make up cell membranes. Substance P is one of the most important and well-studied compounds; it is believed that this chemical binds to receptors on the secondary neuron and elicits an action potential in that neuron, causing the nociceptive message to be transmitted within the central nervous system (Paice, 1991).

The inhibitory process is mediated by neurotransmitters--endorphins, serotonin, and enkephalin. Endorphins stimulate the periaqueductal gray, which stimulates the nucleus raphe magnus to release serotonin (via axons in the dorsolateral column) in the spinal cord. Serotonin in turn stimulates the release of enkephalin by the interneurons in the substantia gelatinosa, which then prevents the A-delta and C fibers from releasing their neurotransmitter, substance P. Without substance P, the pain fibers cannot stimulate the anterolateral system and pain cannot be perceived (Schneider & Tarshis, 1986).

The Study of Pain in Infants

Several issues arise in studying pain in infants that differ significantly from studying pain in adults. One major concern is the need to protect the rights of infant subjects since it is impossible to obtain informed consent from them. Pain cannot be experimentally induced as in adults; however, numerous opportunities exist to observe infants' responses to pain produced as a result of medical procedures, such as circumcision, injections, heel lances, and surgery. These

procedures produce tissue damage that is expected to cause pain in adults (Owens, 1984). However, strict control of the pain stimulus is more difficult when painful procedures are used, making comparisons of results among studies not always possible. For example, technician competence can affect pain intensity (Grunau & Craig, 1987).

In adults, self-report is the most reliable and valid indicator of pain. Pain assessment and pain measurement are sometimes considered different concepts with assessment referring to all strategies of analyzing responses to noxious stimuli and measurement, being concerned only with quantitative methods to measure pain intensity (McGrath & Unruh, 1987).

With infants, self-report is impossible and pain must be inferred from observed changes in response to stimuli considered painful by older children and adults. Therefore, pain measurement, as well as validating memory of pain, is not possible. Izard (1982) proposed the following classification of infant emotional responses, such as physical distress: (1) behavioral, including facial expression, vocalizations, crying, gaze patterns, posture-movement, and autonomic responses (heart rate, respiratory rate, blood pressure, and sweating); (2) biological, including, neurological and endocrinological events; and (3) experiential, including thoughts, the "felt emotion," and images.

The first two categories provide a useful framework for studying infant pain; the third category requires self-report and is not appropriate. Of interest, Sanders (1979) suggested a trimodal classification of adult pain responses that is remarkably similar to that of Izard and includes: (1) gross motor, including complaints of

pain, crying, grimacing, and distorted walk; (2) physiological, including neurological events; and (3) cognitive, including thoughts, feelings, and images. Like Izard's model, cognitive responses do not apply to preverbal children. In the present study, both classifications have been modified as follows: (1) physiological, specifically including heart rate and oxygen saturation, and (2) behavioral, specifically including facial expression and cry.

The extant theoretical literature on pain in infants is extremely limited. However, one theory, differential emotions theory (Izard, 1977, 1982), suggests that in newborn and very young infants, pain will release preprogrammed affective-expressive behavior, a species-common aspect of coping. It also suggests that in normal development, new emotion expressions indicating higher level adaptive responses are more the result of maturation than experience.

These propositions were tested in a study by Izard, Hembree, Dougherty, and Spizzirri (1983), who hypothesized that (a) in younger infants acute pain would typically result immediately in a facial expression of physical distress (i.e., a specific and consistent pattern of facial movements or appearance changes) and (b) with increasing age expressions of physical distress would be less common and of anger more common in response to pain.

Differential emotions theory also maintains that there are wide individual differences in emotional thresholds, that pain activates emotion, and that pain-emotion interactions can amplify and sustain the overall negative affective experience. Thus, the ability of the infant to be soothed ("soothability") following pain is assumed to be more a function of the characteristics of the individual's emotional

system than of age. Four additional assumptions are:

1. Infants' emotional expressions correspond to their emotional experiences.

2. Although the anticipation of pain frequently activates the emotion of fear, pain itself, particularly unanticipated pain, activates a pattern or sequence of negative emotions that typically includes anger.

3. Once pain activates emotion, pain-emotion interactions can influence the course of perturbation.

4. There are wide individual differences in emotional thresholds and hence in pain-emotion interactions and soothability.

These assumptions were tested also in the 1983 study by Izard and colleagues, who hypothesized that there would be a wide range of individual differences in soothability and that fast and slow soothers would show different patterns of affect expressions. The results of these studies are presented under Behavioral Evidence of Pain in Infants. In the present study, the coding of facial expressions in response to an injection used Izard's method, the Maximally Discriminative Facial Movement Coding System (Max) that is based on differential emotions theory (Izard, 1982). The findings of the present study were also examined in light of the theory.

The principal limitations of using behavioral and physiological variables is their lack of specificity for pain. Several stressors other than pain can elicit similar changes. Anxiety causes several responses such as increased heart rate, respiratory rate, blood pressure, cortisol levels, and crying, that are indistinguishable from pain. An advantage in using facial expression as a pain indicator is

its specificity for pain. Fear, a component of anxiety, elicits a different facial expression from pain (Izard, 1982).

Even those responses not specific for pain can strongly suggest a pain reaction for two reasons. First, when a noxious stimulus is produced, tissue damage occurs that predictably results in the same physiological and behavioral responses in adults who can verbally quantify pain intensity. Second, the timing of the response to the noxious stimulus provides strong evidence of cause and effect. For example, when a needle pierces the skin of a calm infant and within moments the infant cries, demonstrates significant physiological changes, and has a facial expression of physical distress, it is logical to assume that these responses indicate a painful event.

However, physiological and behavioral responses do not consistently display the same pattern following a noxious stimulus. For example, heart rate generally accelerates with aversive stimuli, but decelerates with alerting or orienting stimuli (Field, 1982). Consequently, the novel aspects of a noxious stimuli may diminish its aversive quality, thus causing the heart rate to decrease, rather than increase. Sucking and crying also cause the heart rate to increase (Nelson, 1979) and the respiratory rate to increase (Brown, 1987).

Age is also an important factor; premature and/or sick infants may be physically incapable of producing responses such as palmar sweating, motor movement, or cry. In such cases, the number of variables available for assessing pain are reduced, and invasive methods, such as using blood samples, may be the only option, but are impractical for most clinical and research purposes. thus, a multidimensional approach to pain assessment using physiological

and behavioral responses offers more appropriate research framework.

Pain Mechanisms in Infants

It has long been thought that because nerve pathways are not completely myelinated at birth, infants do not experience pain and do not remember the painful event (Swafford & Allen, 1968). McGraw's (1941) study of the neural maturation of the infant lent support to this belief, since her investigation of the newborn's response to a pinprick showed either no response or only a reflexive generalized movement. However, those findings have been disputed with more precise measurements of pain response in the neonate and as neural transmission of pain has become better understood.

Complete myelination of nerve pathways is not required for pain transmission; C fibers are unmyelinated and A-delta fibers are thinly myelinated. Incomplete myelination merely imples a slower conduction velocity in the nerves or central nerve tracts of neonates, which is offset by the shorter interneuron and neuromuscular distances traveled by the impulse (Anand & Hickey, 1987). In addition, complete myelination of the pain pathways to the brain stem and thalamus occurs by 30 weeks gestation, and from the thalamus to the cortex by 37 weeks. Functional maturity of the cerebral cortex is supported by measurements of cerebral glucose utilization, which show maximum metabolic activity in the sensory areas of the brain, especially those believed to be associated with pain sensation (Chugani & Phelps, 1986).

Nociceptive nerve endings are present in all cutaneous and mucous surfaces by the 20th week of gestation, and their density in the

newborn is similar to or greater than than in adult skin (Anand & Carr, 1989). In fact research has shown that the threshold for responding to cutaneous stimulation is lowest in the youngest neonates. Fitzgerald, Shaw, and MacIntosh (1988) tested the somatosensory function of 103 infants; 75 were preterm (tested at 27.5 to 39.5 postconceptional age) and 28 were fullterm. They evoked the cutaneous flexor reflex to test threshold, sensitization, and habituation. By applying von Frey hairs (nylon monofilaments of graded thicknesses, which, when pressed on the skin, produce forces ranging from 0.003 g to 90 g) to the lateral plantar surface of the foot, the researchers measured the reflex, exhibited as a distinct withdrawal of the leg. The youngest infants had the lowest threshold, indicating that much less stimulation was needed to evoke a response. Repeated stimulation of the foot in preterm infants resulted in sensitization of the flexion reflex up to about 32 weeks postconceptional age. After that age, repeated stimulation resulted in habituation, as is observed in the adult. The authors suggest that this low threshold and sensitization result from lack of inhibitory control in the immature spinal cord.

Substance P and its receptors appear in the dorsal-root ganglia and dorsal horns of the spinal cord at 8 to 14 weeks of gestation. Functionally mature endorphinergic cells have been observed at 20 weeks of gestation. The density of all of these substances gradually increases during gestation with marked increases during the perinatal period. Other substances such as the catecholamines appear during late gestation and early infancy (Anand & Carr, 1989).

birth. Newborns respond differently to a pain stimulus depending on their sleep-awake cycle (Grunau & Craig, 1987), and demonstrate the ability to remember pain by responding differently to successive painful stimuli (Fitzgerald, Shaw, & MacIntosh, 1988; Barba et al., 1991) (see section on Issues in Assessing Infant Pain). Thus, newborn infants, even those born prematurely, have the anatomical and functional components required for the perception of painful stimuli, and evidence suggests that they possess higher cognitive functions, such as modulation and memory of pain.

Memory of Pain in Infants

Although the evidence strongly supports the view that physiological pain mechanisms in infants are functional, enabling neonates to react to pain, a question that remains almost unexplored is their remembrance of pain. One reason for addressing this issue is that as this evidence has mounted, opponents of using pain reducers suggest that pain has two aspects. One is conscious perceived pain, which is felt, feared, and remembered. The other is physical effects of pain on the body. They argue that there is little evidence that infants remember pain, so there is no moral reason for relieving it (Campbell, 1989). They further contend that recovery from painful procedures, such as circumcision, is rapid and without consequence. Therefore, pain reducers, such as drugs, add an unnecessary element of risk (Schoen, 1990; Schoen & Fischell, 1991).

Only one study has directly addressed the question of infants' memory of pain. Barba et al. (1991) hypothesized that a repeated

painful experience may cause the newborn to eventually recognize the activities of the event and demonstrate early memory capacities. They analyzed the behavioral and physiological responses of 20 fullterm newborns to repeated heel lancing. With another 20 fullterm newborns as a control group, they repeated the exact same steps of the heel lance procedure but without puncturing the skin. As hypothesized, the experimental group demonstrated responses indicating awareness of the forthcoming painful event, whereas the control group did not. These findings seem to indicate infants' memory of events and their ability to perceptually categorize information.

Indirect evidence for infants' memory of pain is found in two published case histories. Both children were born prematurely and spent extended time in an intensive care unit, undergoing repeated painful procedures. Both children subsequently developed an aversion to human contact. The physician parents of one infant described their son's irritability and crying when others attempted to cuddle, caress, rock, or hold him. The child was most comfortable lying alone in his crib for the first six months at home. The parents believed that premature infants acquire an aversion to human contact because they associate it with pain (Langland & Langland, 1988).

The second study appears to confirm this belief. The infant had been hospitalized from birth for six months for numerous painful medical conditions and was withdrawn, non-communicative, had no eye contact, and was developmentally at 3 1/2 months of age. Those caring for this child speculated that through the process of stimulus generalization, the infant had equated all human contact with negative stimulation and responded by withdrawing and crying. To help the

infant learn to discriminate between pleasant and unpleasant experiences, auditory conditioning was used. The conditioning stimulus (white noise) did not accompany pleasant experiences.

Within a few weeks the infant cried before the unpleasant contact, but was not agitated during pleasant contacts. Within 5 months, his development improved but remained below the expected norm (Sexson, Schneider, Chamberlin, & Sexson, 1986).

Nurses' anecdotal reports suggest that infants show memory by exhibiting defensive behaviors when painful procedures are repeated. Nurses often describe infants who stiffen when touched because human touch has repeatedly been associated with pain. Such infants often become hypervigilant, gazing intently at the hands of people who approach them, rather than at the eyes (Penticuff, 1987). Not only do these reports indicate infants remember painful events, but they also show that continual exposure to pain affects development, especially in response to human contact.

Evidence of Pain in Infants

In the past decade, interest in infant pain has resulted in numerous studies devoted to identifying physiological and behavioral indicators of infants' responses to painful stimuli. Most of the research in this area has measured physiological and behavioral responses procedures that are a part of medical care, such as heel lancing, injections, circumcision, and major surgery. Some studies are descriptive in that they report the changes observed in the subjects during the painful event. Other studies are experiemental in

that they compare the responses of treatment and control groups of infants to a painful stimulus, with the treatment group receiving some type of pain reducer. The following review of research focuses first on studies that investigated the physiological responses to pain during different painful events, and later on the behavioral responses to pain during such events. This division of research is somewhat artificial in that many studies included both behavioral and physiological variables in their measurement of infants' responses to pain.

Physiological Evidence of Pain in Infants

Acute pain elicits a physiologic stress response that includes symptoms such as increased sweating, blood pressure, heart rate (pulse), respiration, and oxygen utilization, as well as chemical changes (McCaffery & Beebe, 1989; Whipple, 1990). Several studies provide evidence for the occurrence of these physiologic responses to pain in infants.

Heel Lance. Heel lance provides one avenue for investigating infants' responses to a painful stimulus. A disadvantage is that heel lance technique can affect pain intensity. Heel lances for metabolic screening tests require not only puncturing of the skin but also squeezing of the heel for an adequate blood sample. Heel lances for a glucose measurement require little or no squeezing, causing less pain.

Harpin and Rutter (1982) studied the development of emotional sweating in 124 infants of gestational age 25-41 weeks and postnatal age 15 hours to 9 weeks. They had hypothesized that sweating from the

palm of the hand and sole of the foot which is triggered by emotional factors (increased by pain, fear, anxiety, and concentration, and decreased by contentment, relaxation, and sleep) might be valuable in determining infants' responses to pain. To measure palmar sweating they used an evaporimeter, an instrument that measures the water vapor pressure gradient close to the skin surface to estimate water loss from the skin. In infants of 37 weeks of gestation or more there was a direct relationship between palmar sweating and arousal. By 43 weeks gestation, the amount of emotional sweating reached levels found in anxious adults.

Next, Harpin and Rutter (1983) compared the sweating responses of 36 full-term newborns to a heel lance for metabolic screening using a metal lancet or a mechanical lancet (Autolet). Measurements were recorded before the lance, when infants were either asleep or quietly awake, during the heel lance and squeezing, and until the palmar water loss returned to resting levels. Significantly less palmar sweating occurred in the group with the Autolet device; 3 infants slept during the procedure and 2 infants, while awake, remained quiet with no increase in palmar water loss. No such infants were found in the control group.

Changes in response to heel lancing for metabolic screening with respect to palmar sweating, heart rate, respiratory rate, systolic blood pressure, and oxygen saturation were also studied in 52 fullterm infants by Schwartz and Jeffries (1990). An evaporimeter was used to measure palmar sweat as an index of pain; the other physiologic measurements were monitored automatically at 1-minute intervals. Measurements were taken before the heel lance, during cleaning of the

heel, during heel lancing, and post-heel lancing. Statistically significant differences were found in all measurements during the different stages of the procedure. However, only changes in palmar sweating, heart rate, respiratory rate, and oxygen saturation were consistent. Palmar sweating and heart rate increased, while respiratory rate and oxygen saturation decreased. Changes in systolic blood pressure were inconsistent and were probably due to the inability of the monitoring device to measure blood pressure accurately at frequent intervals and during patient movement. Findings were generally consistent with those of other research with the exception of respiratory rate. Respiratory rate decreased, especially during heel lancing when crying was associated with breath holding and gasping, but increased during the post-heel lancing as the infants recovered.

Norris, Campbell, and Brenkert (1982) investigated changes in transcutaneous oxygen during three nursing procedures, suctioning, repositioning, and heel lancing, on 25 infants born before 30 weeks gestation. Changes in oxygenation were measured transcutaneously by placing a special heated electrode on the infant's skin to determine the tension of oxygen diffusing from the arterialized capillary bed to the skin surface. Significant decreases in transcutaneous oxygenation occurred following suctioning and repositioning, but not heel lancing. As expected, the greatest change occurred with suctioning immediately following the procedure. Once suction is applied, not only are endotracheal secretions removed, but oxygen is also removed from the airway. Changes in repositioning may also have been partly due to the fact that the airway can be partially occluded when the head is moved.

During the heel lance, only one foot and heel are touched, compared to the disruption of a greater body surface area with suctioning and repositioning. Another factor that may affect infants' responses is their state; suctioning and repositioning are more likely to fully arouse infants than a quick skin puncture; unlike the other studies cited above, this heel lance was used to obtain one drop of blood for glucose testing, avoiding the need to squeeze the heel. However, it is possible that premature infants are unable to mount the same physiologic responses, such as vigorous crying which depletes the oxygen supply, as fullterm infants are able to do.

Additional evidence on the responses of fullterm newborns and premature newborns was provided by Field and Goldson (1984). Behavioral state, heart rate, and/or respiratory rate during heel lance was studied in 48 healthy, fullterm neonates, 48 preterm neonates treated in a minimal care nursery, and 48 preterm neonates treated in an intensive care nursery. Infants in the treatment group were given a pacifier that was held in the infant's mouth by a research assistant for the duration of the observation period, which included 2 minutes before the heel lance procedure (baseline), for the duration of the procedure, and for 2 minutes following the procedure. Significant increases in heart and respiratory rates during the heel lance followed by decreases in both of these measures during the recovery phase occurred in the preterm neonates receiving minimal care but not in the neonates in intensive care. Also, the use of the pacifier significantly attenuated increases in heart and respiratory rates in the preterm infants receiving minimal care but not in infants in intensive care. Gestational age and severity of illness appear to

influence infants' physiological responses to pain. Of interest, the infants in intensive care demonstrated significantly less behavioral distress, suggesting that behavior and autonomic function may not be closely coupled in sick premature infants.

Owens and Todt (1984) compared changes in heart rate and crying in a group of 20 fullterm newborns in response to a heel lance, noninvasive tactile stimulation (rubbing the heel with alcohol), and the baseline periods for these two events. Heart rate was electronically monitored and was significantly increased during both the heel lance and tactile stimulation phases over the baseline phase; heart rate was also significantly higher in the heel lance phase as compared to the tactile stimulation phase. The mean increase in heart rate was 49 beats/minute (SD = 17.5) and the mean duration of the increase was 217.6 seconds. However, there was wide variability among the 20 children.

Brown (1987) also monitored blood pressure, transcutaneous oxygen, heart rate, and respiratory rate of 17 fullterm infants during a heel lance used to draw a blood sample to test for phenylketonuria (PKU). All of the variables were monitored electronically. Baseline measurements of these variables were taken before the child was disturbed and then recorded for 2 to 5 minutes. All of the physiological parameters returned to baseline by 5 minutes. Statistically significant differences in transcutaneous oxygen, systolic blood pressure, and respiratory rate were found in response to the painful stimulus. No significant differences were found between diastolic blood pressure and heart rate.

Finally, Stevens (1991) measured heart rate, oxygen saturation,

and intracranial pressure in 8 infants with a mean age of 33 gestational weeks. Physiologic parameters were continuously monitored from 30 seconds before beginning the procedure through heel warming in a cup of water, heel lance, heel squeeze, and application of a bandaid until the variables returned to baseline following the procedure. The results indicated that all parameters changed significantly but differently during various phases of the heel puncture. Stevens found that heel squeeze was significantly different from baseline and heel warming on all parameters but was not significantly different from heel stick, suggesting that heel squeeze is also a painful part of the procedure. In her study, intracranial pressure returned to baseline first, followed by heart rate and later by oxygen saturation. Although oxygen saturation required the longest time to return to baseline, Norris, Campbell, and Brenkert (1982) found that oxygenation, measured transcutaneously, did not change significantly during any phase of the heel lance. This difference again may be due to the way blood was sampled.

All of these studies investigated acute responses to a single heel lance. However, Fitzgerald, Millard, and McIntosh (1989) analyzed the response of 17 premature infants born at 27 to 32 weeks gestational age to repeated heel lances by using the flexion reflex. The flexion reflex is a nociceptive reflex involving withdrawal of a limb from a stimulus, that in this study consisted of calibrated von Frey hairs (nylon hairs of graded diameter that when pressed onto the skin apply different forces). Over time the reflex occurred in response to decreasing force from the hairs, indicating that the infant became hypersensitive to pain. When a topical anesthetic was

applied to the heel before the puncture, the reflex threshold did not decrease. This important study demonstrated that premature newborns' nervous systems are capable of mounting a chronic stress response, and that at the earliest ages of life children do not habituate to painful stimuli.

Injection. Injectable vaccines are a routine part of well-child care and several studies have measured various physiological and behavioral responses to this stimulus. Two important differences exist between studies using heel lance or injection. One difference is age of the subjects. In heel lance studies, all of the subjects were newborns, whereas in the injection studies, the subjects ranged from at least two months to 24 months old. Another difference is that the injections may provide more consistent stimuli than heel lances.

Johnston and Strada (1986) studied the responses of 14 infants ages 2 to 4 months receiving routine DTP immunization. They measured heart rate, crying, body movement/posturing, and voice spectrograph. Heart rate was continuously monitored using ECG and was analyzed at 3-second intervals. Recordings of the variables were made 30 seconds before and 45 to 60 seconds postinjection, depending on how quickly the infant settled and the parents wished to leave the examination room.

Heart rate changed in relation to the phases of the injection procedure. During the first 3 seconds following introduction of the needle into the child's arm, heart rate decreased for 9 subjects, remained the same for 3, and increased for only 2. The average decrease in heart rate at this time was 24 beats per minute (range of heart rate was 153 to 167). Four infants' heart rates dropped as much

as 80 to 90 beats per minute. The heart rate began to increase past this 3-second period, and during the next 27 seconds of the injection phase, the heart rate averaged 184 beats per minute with a range of 160 to 220. Only one infant did not have an increase in heart rate. During the second 30 seconds of the postinjection phase, the heart rate remained elevated and averaged 182 beats per minute.

Dale (1986) examined 10 infants' responses to their first or second DTP injections. Five infants received the first DTP injection at 2 months of age and 5 infants received the second DTP injection at 4 months of age. Heart rate was not automatically and continuously monitored, but was taken at 3 times: before injection, immediately after injection, and approximately 2 minutes after injection. Eight infants had increased heart rates from the first to the second measure and two had decreased rates. The heart rates of 6 infants decreased from the second to the third measure; three increased and one remained the same.

Another study provided information on the change in cortisol in response to the stress of an injection (Lewis and Thomas, 1990). Changes in levels of cortisol have been studied as a measure of stress (see section on major surgery), but a major disadvantage has been the need to obtain serial blood samples for comparison. Sixty-nine infants aged 2, 4, and 6 months had their saliva cortisol measured approximately 10 minutes before receiving a DTP immunization and 15 minutes following the inoculation. No age differences were found in the preinoculation cortisol values, and postinjection cortisol values were significantly elevated only in the 2 month-old subjects. Also, 2 month-old infants showed greater rises in the stress response and a

longer time until calming than the 4- and 6-month-old children.

Circumcision. Circumcision is performed on most newborn males in the United States and has been used as a pain stimulus in numerous studies. In early studies, responses to circumcision performed without anesthesia were described. However, later studies compared pain responses in infants who did or did not receive local anesthesia, typically dorsal penile nerve block (DPNB), during circumcision. These studies are reviewed below.

Disadvantages to using circumcision as a noxious stimulus are that the type of procedure used to remove the foreskin and operator competence may influence the severity of pain (Gunnar, Fisch, & Malone, 1984; Gunnar, Malone, Vance, & Fisch, 1985). In the studies reviewed, the Gomco clamp procedure was almost always used, but in several studies multiple practitioners performed the surgery. Also, the DPNB, although effective in reducing pain, is not an "all or none" intervention. Success with this technique varies according to operator competence and the infant's anatomy (Holve et al., 1983).

Williamson and Williamson (1983) analyzed the responses of 20 infants receiving circumcision with DPNB to 10 infants receiving circumcision without DPNB. Heart rate was continuously monitored using electrocardiography (ECG) and respiratory rate was continuously monitored using pneumography. Significant differences between groups occurred during dissection of the foreskin and attachment of the Gomco clamp in heart rate (increased more in unanesthetized group) and blood oxygenation (decreased more in unanesthetized group); significant differences in heart rate also occurred during removal of the clamp. No significant differences were found for respiratory rate. With the

exception of crying and blood oxygenation, there were no significant differences in the other variables during the period of injecting the local anesthetic, a potentially painful procedure. Therefore, the pain of the injection was not so great as to mask its effect in decreasing the discomfort of the circumcision.

Holve et al. (1983) compared the use of DPNB in 15 newborns (DPNB group) to the use of saline injection in 8 infants (saline group) and circumcision without DPNB or saline in 8 additional subjects (no injection group). Heart rate was continuously monitored via ECG during 6 stages of the circumcision, beginning with a baseline determined after restraint and ending with removal of the Gomco clamp. Significant differences in heart rate occurred during the clamping procedures, with the DPNB group having lower rates than the other two groups. No significant differences were found between the three groups during injection of the local anesthetic or saline or clamp removal. However, the use of a baseline calculated after restraint is a possible weakness in this study. As Williamson and Williamson (1983) showed, the restraint procedure causes dramatic changes in heart rate and cry that could have masked the significance of subsequent changes in such variables.

Maxwell, Yaster, Wetzel, & Niebyl (1987) compared heart rate, blood pressure, and oxygen saturation in 20 newborns being circumcised with DPNB and 10 infants being circumcised without an anesthetic. Heart rate and oxygen saturation were monitored continuously with ECG and pulse oximetry for six minutes before and for the duration of the circumcision. Systolic blood pressure (BP) was measured by Doppler every five minutes, from the time the subject was restrained to the

end of the procedure. All variables were also measured 15, 30, and 60 minutes after the start of the circumcision (five minutes after the DPNB or after restraining the unblocked subjects). Baseline values for all three variables were calculated after the infants were restrained but before the DPNB was done.

The changes in the three variables were compared at baseline, for the circumcision as a whole, and at 15, 30, and 60 minutes from the start of the procedure. Significant differences occurred in heart rate and oxygen saturation, but not blood pressure, during the circumcision only. The heart rate rose 34% during circumcision in the unanesthetized infants and did not increase significantly from baseline in the anesthetized group. The decline in oxygen saturation in the unblocked group was 16% compared to 6% in the blocked group. The surgeons, who were unaware of the anesthetic status of the infants, correctly identified all ten controls as unanesthetized and 16 of the 10 blocked infants as anesthetized.

Lidocaine is the standard anesthetic agent used for DPNB. One disadvantage to its use is the required waiting period of five minutes for the drug to induce anesthesia. Since this waiting time is almost as long as the circumcision itself, physicians may be reluctant to use DPNB or may use it but fail to wait until its effect occurs. To evaluate the effectiveness of a shorter-acting anesthetic (chloroprocaine), Spencer et al. (1992) compared the responses of five groups of 15 newborns each to circumcision without anesthesia; with DPNB using lidocaine and a 5-minute wait; and with DPNB using chloroprocaine and a 2-, 3-, or 5-minute wait. Heart rate, oxygen saturation, and cry were monitored before the procedure (baseline) and

during 6 stages of the circumcision. Seven residents and twelve medical students performed the blocks and circumcision. All infants were given pacifiers during the procedures.

Heart rate was taken from the display on the pulse oximeter. Changes from baseline were almost always decreases at all stages of the circumcision and for all five groups, a dramatic departure from findings on heart rate in all other studies. Among the negative excursions from baseline, differences in heart rate occurred between the control group and the chloroprocaine 2- and 3-minute wait group during lateral clamping and between the control group and chloroprocaine 2-minute wait group during foreskin cutting, with less excursions from baseline in the anesthetic groups. The authors concluded that the DPNB modestly reduced the stress in circumcision and that chloroprocaine with a 2- or 3-minute waiting time was as effective as lidocaine with a 5-minute waiting time. Although these conclusions are somewhat supported by the data, the unexpected decrease in heart rate weakens the findings.

Besides DPNB, a second approach is to locally anesthetize the tissue at the operative site, the corona of the glans. Other than the different puncture sites, the infiltration procedure is identical. Masciello (1990) compared heart rate, oxygen saturation, cry, and cortisol levels among three groups of infants. Ten infants received DPNB, 10 received local anesthesia, and 10 served as unanesthetized controls. Heart rate and oxygen saturation were continuously monitored with ECG and pulse oximetry. Baseline values were obtained after the infant was restrained and recordings were taken during administration of anesthesia, 5 minutes after administration of

anesthesia (or after restraint for controls), during 5 steps in the circumcision, immediately after circumcision, and 5 minutes after circumcision. Cortisol levels were measured 30 minutes after circumcision.

As in the previous studies, heart rate and oxygen saturation were significantly different in the two anesthetized groups as opposed to the unanesthetized group during the more painful stages of the circumcision. During administration of the two types of anesthesia, heart rate increased and oxygen saturation decreased but these changes were not significantly different from the control group.

However, significant differences for the 2 anesthetic groups were found for three steps of the circumcision procedure. The local anesthetic group had smaller changes in heart rate and oxygen saturation than the DPNB group for dissection of the foreskin and placement and clamping of the Gomco, suggesting better anesthesia on the ventral surface of the penis.

Cortisol levels were significantly lower in the local anesthesia group as compared to the control and DPNB groups. Although this finding also suggests better pain control in the local anesthesia group, a major weakness in the study is the lack of a baseline value. As the study by Lewis and Thomas (1990) showed, baseline cortisol values can exert a significant effect on the subsequent change in the cortisol levels.

Attempts to reduce pain during circumcision have also included noninvasive techniques, such as applying a local anesthetic ointment on the penis. Mudge and Younger (1989) analyzed the responses of 20 infants receiving a topical anesthetic (4% lidocaine in acid mantle

cream) and 24 control infants receiving only acid mantle cream 2 hours before circumcision. Heart rate, respiratory rate, oxygen saturation, cry, and general responses to the circumcision were measured. Heart rate, respiratory rate, and oxygen saturation were continuously monitored using ECG, pneumography, and pulse oximetry, respectively, during 5 events: (1) before the infant was restrained (baseline); (2) 30 seconds after the initial bilateral clamping of the foreskin and initial cutting of adhesions; (3) 30 seconds after dissection of adhesions and placing of the Gomco clamp; (4) 30 seconds after securing the clamp; and (5) 30 seconds after loosening the clamp. Heart rate was significantly lower during events 2 through 5 in the treatment group.

Researchers have also investigated the effectiveness of nonpharmacological techniques in reducing pain responses during circumcision. Marchette, Main, and Redick (1989) measured the effect of two comfort interventions. Fifteen infants listened to classical music, 15 infants listened to intrauterine sounds, and 18 infants received routine care without these comfort measures. All subjects were circumcised without anesthesia. Facial expression and alertness were also measured. The circumcision was divided into 11 steps, beginning with strapping the subjects to the restraint board and ending with removal of the clamp. Mean heart rate of the control group was above normal limits (>180 beats/minute) for all stages of the actual circumcision except for Gomco removal. Mean heart rate of the comfort groups was slightly lower during some of the steps but no significance tests were reported. Mean systolic BP differed significantly between the control and comfort groups only during the

2-minute wait period after the Gomco clamp was tightened. The authors concluded that the two comfort measures were ineffective in reducing the stress of the circumcision.

In a larger study employing 121 newborns undergoing unanesthetized circumcision, Marchette, Main, Redick, Bagg, and Leatherland (1991) evaluated the effectiveness of 5 comfort interactions: (1) classical music, (2) intrauterine sounds, (3) pacifier, (4) classical music and pacifier, and (5) intrauterine sounds and pacifier. A sixth group receiving no comfort measure served as the controls. Essentially the same measures were taken as in their previous study. The findings were basically the same and the authors' drew the same conclusion -- nonpharmacological interventions were not sufficient to reduce the severity of pain associated with circumcision.

Several studies have used changes in cortisol as a measure of distress following circumcision. Gunnar, Fisch, and Malone (1984) measured 18 newborns' behavioral and adrenocortical responses to unanesthetized circumcision. Three different circumcision procedures were performed by seven different physicians, including four residents. Half the subjects were given a pacifier as a comfort measure and half were not. Serum cortisol levels were determined immediately before circumcision and 30 minutes later.

Both groups evidenced a striking elevation in serum cortisol 30 minutes after onset of circumcision, and the changes were unrelated to the use of a pacifier. Changes in postcircumcision cortisol levels were also significantly related to the type of surgical procedure. The standard method, which involved clamping the foreskin, then

waiting 5 to 6 minutes before removing the foreskin, caused less of a rise in cortisol than the modified method which eliminated the waiting period. The authors suggested that the standard procedure may be less aversive because the waiting period allows the infant to calm. Indeed, this explanation is supported by similar findings, such as mean heart rate and systolic blood pressure being lower during this waiting period, in the Marchette, Main, and Redick (1989) study.

Gunnar, Malone, Vance, and Fisch (1985) analyzed change in cortisol levels over 5 points in time in 90 infants undergoing unanesthetized circumcision. First, 80 newborn males were assigned randomly to one (n = 10) of 8 groups, representing the complete crossing of the following factors: type of circumcision (Gomco clamp vs Plastibell) and postcircumcision plasma cortisol time points (30, 90, 120, and 240 minutes timed from baseline cortisol samples taken just before the start of the circumcision). An additional 10 subjects were randomized into 2 groups by type of circumcision at 150 minutes.

As in their previous studies, the authors found significant increases in cortisol after circumcision, with the peak rise occurring at 30 minutes and baseline being reached at approximately 150 minutes. Cortisol levels did not vary significantly by type of circumcision method.

Stang, Gunnar, Snellman, Condon, and Kestenbaum (1988) measured serum cortisol levels in three groups of infants (N = 60) being circumcised. One group (n = 2) was unanesthetized, another group (n = 20) received a DPNB using lidocaine, and a third group (n = 20) received a saline injection simulating a DPNB. Plasma cortisol levels were measured in half of the subjects in each group at 30 minutes

after being restrained for the circumcision; the other half were sampled at 90 minutes after being restrained.

For all three groups cortisol levels were significantly elevated over the baseline and were higher at 30 minutes than at 90 minutes. At 30 minutes the lidocaine and saline groups differed significantly. Overall, the levels of cortisol were lower in the lidocaine group as compared to both control groups when the data for the 2 sampling times were averaged.

Williamson and Evans (1986) compared cortisol levels in 13 infants receiving circumcision without anesthesia and 11 infants receiving circumcision with DPNB. Baseline cortisol levels were taken before the lidocaine injection and the second samples were taken 30 minutes after the clamp was applied. Both groups demonstrated a significant but similar rise in cortisol levels.

Finally, Porter, Porges, and Marshall (1988) have provided evidence of neurological changes in the newborn associated with the stress of unanesthetized circumcision. They hypothesized that the increases in pitch of cry commonly heard in stressed infants result from decreased vagal tone. Normally, the vagus nerve helps control the tension of the laryngeal musculature by preventing contraction of the laryngeal muscles. During stress or damage to the parasympathetic nervous system, the inhibitory effect of the vagus nerve on the contraction of laryngeal muscles is decreased, resulting in a characteristically high-pitched cry.

Vagal tone was measured in 32 infants undergoing circumcision without anesthesia. Vagal tone was measured by the amplitude of respiratory sinus arrhythmia as calculated from the ECG.

Vocalizations were continuously audiotaped. Two features of the vocalizations were analyzed with a sound spectrograph: (1) cry duration (time from onset to the end of the first expiratory cry) and (2) fundamental frequency (the lowest tone of a complex waveform or the number of hertz between any two successive harmonics). Heart and respiratory rates and vocalizations were monitored for five periods: 10 minutes preoperatively (baseline), 5 minutes during preoperative restraint, 10 minutes of the circumcision (divided into 7 steps), 5 minutes of postoperative restraint, and 10 minutes postoperatively (second baseline). To assess the impact of restraint and the duration of the procedure, a control group of 7 males and 10 females was restrained and monitored for 40 minutes (the equivalent time of the circumcision events) but not circumcised.

Changes in vagal tone were compared for each of the five periods and for each step of the surgery. Vagal tone was significantly lower during surgery than during the pre- and postoperative periods. The lowest vagal tones occurred during dissection of the foreskin and attaching the clamp, the two most invasive surgical procedures. Vagal tone did not differ during pre- and postoperative procedures in the circumcised and control groups, indicating that the circumcised group experienced a prompt physiological recovery.

Vagal tone also predicted cry characteristics and individual responses of the infants to stress. Decreased vagal tones were paralleled by significant increases in fundamental cry frequency and by decreases in cry duration. During the most invasive surgical procedures, peak fundamental frequencies were as high as 800 to 2000 hertz. Also, infants with higher resting vagal tones exhibited

greater changes in vagal tone during surgery, while infants with lower resting vagal tones exhibited smaller changes in vagal tone during surgery. The authors suggested that resting vagal tone may be an accurate index of physiological reactivity in infancy. It is of interest to note that this pattern of change was the opposite of that found with cortisol, where a low baseline was associated with larger changes (Lewis & Thomas, 1991).

Major surgery. Major surgery providesanother means for studying infant pain. Research has focused on the systemic stress responses of neonates to closed heart surgery performed under different types of anesthesia and/or postoperative analgesia.

Anand, Sippell, and Aynsley-Green (1987) investigated the hormonal stress responses in a randomized controlled study of preterm infants undergoing heart surgery. A control group was given a muscle relaxant and nitrous oxide and an experimental group received these agents with anesthesia induced with fentanyl. Compared with the anesthesia group, measurement of hormonal stress responses, particularly levels of adrenalin but also cortisol, glucagon, aldosterone, and insulin/glucagon ratio, were significantly higher in nonanesthetized infants during the surgery. In addition, the control group had more circulatory and metabolic complications postoperatively. A similar study using the anesthetic agent, halothane rather than fentanyl, also showed decreased hormonal responses to the surgery in the anesthetized neonates (Anand, Sippell, Schofield, & Aynsley-Green, 1988).

Anand and Hickey (1992) compared the responses of 45 newborns to different types of anesthesia and postoperative analgesia. In a

randomized trial, 30 fullterm newborns were assigned to receive deep intraoperative anesthesia with high doses of sufentanil and continuous postoperative infusions of either sufentanil or fentanyl for 24 hours; 15 neonates were assigned to receive anesthesia with halothane and morphine followed postoperatively by intermittent intravenous doses of morphine and diazepam. Research has shown that high doses of opioids, such as morphine and sufentanil, more effectively suppress the hormonal stress response than inhalation agents, such as halothane (Anand & Carr, 1989).

Hormonal and metabolic responses to surgery were evaluated by blood samples obtained before, during, and after the operations. The neonates who received deep anesthesia had significantly reduced responses of beta-endorphin, norepinephrine, epinephrine, glucagon, aldosterone, and cortisol. This group also had more severe hypergylcemia and lactic acidemia during surgery and higher lactate concentrations postoperatively. These three studies also demonstrated significantly different outcomes in morbidity and mortality based on the type of anesthesia that the infants received (see Results of Efforts to Control Pain in Infants).

Behavioral Evidence of Pain in Infants

Changes in behavior have also provided significant evidence for the effects of pain in infants. A variety of variables have been investigated, including vocalizations (especially cry), behavioral state, facial expression, and movement. Pain sources have included the same pain stimuli (heel lance, circumcision, and

injections) used for measuring physiological responses, as well as pinprick and multiple painful events. Since many of the studies reviewed in the previous section on physiological evidence of pain in infants also included behavioral variables, the description of the methodology in these studies is only briefly discussed in the following section.

Heel Lance. Several studies in which heel lance was the pain stimulus included cry as a measure of pain. Owens and Todt (1983) found that crying was almost an immediate response to the heel lance. The duration of crying averaged 207 seconds (SD = 118 seconds), and was slightly shorter than the mean duration of elevated heart rate (217.6 seconds). The crying response to the tactile stimulation before the heel lance was much more variable than to the heel lance, suggesting that crying was more likely to occur in response to pain than to mild stimulation.

Although Owens and Todt found no sex difference in newborns's cry responses, Grunau and Craig (1987) found that boys began to cry sooner and cried longer than girls in response to heel lance. State was also related to cry in that infants in quiet sleep had the longest latency to cry. However, fundamental frequency of the initial cry was not related to sleep/wake state, sex, or the amount of facial activity. This indicates that healthy newborns can produce a consistent vocalized response to pain.

Field and Goldson (1984) found that crying decreased in infants receiving a pacifier during a heel lance and concluded that the pacifier was effective in minimizing distress, a finding that is questionable based on results of others who have measured cortisol and

crying (Gunnar, Fisch, & Malone, 1984). However, an important finding in this study was that sick premature infants cried less regardless of the use of a pacifier than minimally ill premature infants or healthy fullterm newborns, suggesting that gestational age and severity of illness influences the ability to cry vigorously. Therefore, crying as a measure of pain may be less useful in this age group.

The results of sound spectrographic analysis of cry on newborns ages 30 to 37 gestational weeks has shown that cries in premature infants are different from those in fullterm healthy newborns. Duration of cry is typically shorter, and pitch is higher in the youngest neonates, but these characteristics change to resemble those of fullterm newborns by 38 weeks of gestation (Michelsson, Jarvenpac, & Rinne, 1983). Therefore, when cry is used to assess pain, gestational age should be taken into consideration.

Grunau and Craig (1987) analyzed the facial expressions of 140 newborns to heel lance for metabolic screening. They developed a coding system to examine facial activity that was unrelated to emotions, as in the Izard system. They found a consistent constellation of facial changes following heel lance, but not heel rub. The "pain" expression included eye squeeze, brow contraction, naso-labial furrow, taut tongue, and open mouth, accompanied by crying. Facial expression varied according to the infant's state; infants in quiet sleep showed the least facial reaction, whereas infants in awake-alert but inactive state showed the most facial reaction. Males reacted more quickly with facial changes than females, a sex finding consistent with that for cry. Technician competence also affected the facial expression during the heel

squeezing phase.

The fact that the subjects responded differently depending on their state suggests that at birth infants have the capacity to modulate their pain response, possibly providing evidence for functioning inhibitory mechanisms as proposed by the gate control theory. Also, it seems that "pain" expressions are remarkably similar regardless of type of coding system used and that facial changes are related to the intensity of the stimuli (rubbing versus puncturing the skin). The heel squeeze is an important source of pain in addition to the puncture, and the operator can influence the intensity of pain.

Finally, one study provided a fine-grained analysis of newborns' motor responses to pain. Using photogrammetric techniques (analysis of videotapes through a calibrated grid) to record the responses of 10 fullterm newborns to heel lancing for metabolic screening, Franck (1986) showed that all of the newborns had an immediate gross motor response of withdrawal of both legs away from the stimulus; 7 infants used the unaffected leg to "swipe" at the lanced site. These findings are in direct contrast to those of McGraw (1941), who found a lack of response in some newborns. However, with the photogrammetric analysis it is possible to detect slight movements that probably went unnoticed in McGraw's study.

A unique finding in Franck's research was the comparison of motor and cry responses to two heel lances, the second one following shortly after the first puncture (the average duration of one or two lances was 3 minutes, 34 seconds). During the second injection the infants cried less and had less motor activity. This finding suggests that pain responses are not additive and the second noxious stimuli in some

way may affect pain transmission and perception. Franck suggested that the mechanism of counterirritation may be responsible for this response.

Injection. Several studies have used injection as a pain stimulus to assess behavioral responses, especially cry, facial expression, and movement of infants. Most of the research subjects have been infants ages 2 months and above who received immunization injections. One study used the routine injection of vitamin K and observed newborns' behavioral responses. This study specifically investigated whether the newborns' (N = 36) responses of facial expression and cry would vary in intensity to three different types of stimulation: injection, rubbing the thigh with alcohol, or applying triple dye solution to the umbilical stump (Grunau, Johnston, & Craig, 1990). Each infant received all three procedures in counter-balanced order; the same nurse performed all three procedures.

Facial expression was scored using the Neonatal Facial Coding System which identified the following movement actions: brow bulge, eye squeeze, naso-labial furrow, open lips, stretch mouth vertical or horizontal, lip purse, taut tongue, tongue protrusion, and chin quiver. Analyses were performed on the occurrence of each facial action, the total facial activity, and the latency to facial movement as identified during the initial 15 seconds of videotaping from the application of each stimulus. A cluster of facial actions comprised of brow bulging, eyes tightly closed, deepened naso-labial furrow, and opened mouth was found significantly more often in response to the injection than to thigh rub or umbilical stump solution. Total facial activity was greater for thigh rub than umbilical stump solution,

suggesting that facial expression, both the anatomic features and the frequency of occurrence, was specific for pain versus non-nociceptive tactile stimulation. Taut tongue was found significantly more frequently during the injection, whereas tongue protrusion occurred more often in the other procedures. The authors suggested that taut tongue in combination with the other cluster of actions may signify greater pain sensitivity or expressivity. Latency to facial movement was also shortest in the injection group.

Several characteristics of cry were analyzed, including time to initial cry, duration, fundamental frequency, melody type, jitter, and phonation. The major findings were shorter latency to cry and longer duration of cry in response to injection. In infants who cried in response to injection and thigh swab, maximum fundamental frequency and intensity of the first cry were also significantly different.

Facial activity was not correlated to cry acoustics, but it was correlated with cry latency and duration. The authors concluded that the facial pain expression accompanied by cry of rapid onset and a first cycle of long duration typified a healthy newborn's reaction to brief invasive events. In addition, taut tongue and high cry pitch and intensity may indicate greater distress.

Unlike the previous study that used the Neonatal Facial Coding System to analyze facial changes in response to pain, Izard developed the Maximally Discriminative Facial Movement Coding System (Max), which is based on differential emotions theory (Izard, 1977, 1982) (see The Study of Pain in Infants). Izard, Hembree, Dougherty, and Spizzirri (1983) tested the theoretical assumptions related to facial expression, maturation, and soothability by identifying the facial

expressions display by infants in response to an injection. The subjects included 9 infants in each of 4 age groups: 2, 4, 8, and 19 months.

Their results supported the hypotheses that in younger infants acute pain would typically result immediately in a facial expression of physical distress and with increasing age the physical distress expression would become less dominant and the anger expression more dominant as an immediate response to pain. The results showed that 16 of 18 infants below 6 months of age displayed the facial expression characteristic of physical distress in response to the injection. At 19 months 6 of the 9 infants showed anger as the first expression change, but 7 of them showed physical distress sometime during the first 10 seconds following needle penetration.

In regard to soothability, the youngest infants (2 months) had the longest soothing times and, as expected, showed predominantly physical distress expressions. When the groups were divided into slow and fast soothers based on a median split of time to soothe (soothing was defined as 5 continuous seconds without crying and with a facial expression of interest or joy), the slow soothers showed more anger expressions, while the fast soothers showed more physical distress expressions.

In a second investigation Izard, Hembree, and Huebner (1987) performed a longitudinal study on 25 infants 2 to 19 months of age to address the question of individual stability of facial expressions and to replicate the basic findings of the 1983 cross-sectional study. The results supported stable individual differences for anger and sadness expressions, but not for pain, interest, or blended

expressions, and reaffirmed the findings from the earlier cross-sectional study.

Johnston and Strada (1986) used the Max to describe the response of 14 infants ages 2 and 4 months to an immunization injection and found that physical distress expressions were the most consistent indicators of pain, occurring in 11 subjects immediately after the injection. The facial expression was accompanied by crying that demonstrated an initial response of long-high pitched cry followed by a period of apnea and then lower pitched cry with some dysphonated cries. In addition, body movements typically included rigidity of the trunk and limbs. The authors commented on the relationship of these behaviors to heart rate during the 1-minute observation period. They found that crying stopped, the facial expression and body movements returned to normal, but the heart rate lagged behind in its return to baseline.

Dale (1986, 1989) also reported on the behavioral responses of 2- and 4-month old infants (N = 30). Using a constellation of facial characteristics similar to those described by Izard, but also adding reddened face and flared nostrils, she found that in the first 5 to 10 seconds immediately after needle puncture, all of the facial characteristics typical of a pain expression were present. By the end of 30 seconds, some of them (eyes closed, nostrils flared) returned to the opposite expression (eyes opened, nostrils not flared). During this time, most of the infants cried continuously, with several of them crying at the end of 30 seconds without facial expressions of distress.

A third study also investigated the behavioral responses of 60

infants ages 2 to 6 months to an immunization injection, but the purpose of the study was to test the effectiveness of a skin coolant in reducing injection pain (Maikler, 1991). Although several excellent analyses were conducted on facial expression (using the Max), body movement, and cry, the results were reported only in terms of the significant differences for the treatment and control groups and in relation to age.

The infants receiving the spray coolant had significantly less startle movement upon needle insertion and longer latency to cry. However, significant age group (less than 16 months vs more than 16 months) differences were found. The duration of the pain expression and of "intense" crying (urgent, arousing, high-pitched, piercing, screaming) was longer in the younger children, whereas the duration of "protest" crying (less arousing, rhythmical, lower pitched, musical) was longer in the older children. Younger children also demonstrated more reflexive symmetrical movement, while older children demonstrated more deliberate protest-like movement, such as patting the thigh or kicking the injected leg. Unfortunately, the data for the three age groups was analyzed using analysis of variance with age categorized into 2 groups. While this statistical analysis identified group differences, it did not reveal trend differences which could have occurred among the 2-, 4-, and 6-month age groups.

Lewis and Thomas (1990) measured cry and facial expression in 69 infants ages 2, 4, and 6 months during a vaccination injection and compared the behavioral measures to cortisol responses. Unlike other studies that used previously developed facial coding systems, they developed their own criteria based on a scale of 0 - 3. They used the

same approach for coding cry and combined the scores to reflect one behavioral score (range 0 - 6). Significant age differences were found for latency to quiet, defined as two consecutive 5-second blocks at a level 2 below the highest response for the subject (total observation time from needle insertion was 90 seconds). Six-month-old infants exhibited a significantly shorter time to quiet than 2-month old infants, with 4-month-old infants in between the two groups. Behavioral distress was also related to postinjection cortisol levels in that children who had rises in cortisol demonstrated significantly more initial reactivity (level of behavior response during the first 5-second block) than children who had decreases in cortisol.

While several studies have qualitatively analyzed cries in response to injection pain, Fuller (1991) studied quantitative acoustical characteristics of three types of infant cries: pain-induced, hunger, and fussy. The sample was 21 infants ages 2 and 4 months old. Based on computer analysis of several acoustical features, the results showed that pain-induced crying was associated with significantly greater highest and lowest second formant amplitudes (a formant is the accentuated portion of a voice spectrum; the frequency of a formant designates its position in the spectrum while the amplitude reflects the formant's energy) as compared to hunger or fussy crying. Fussy crying was associated with significantly less tenseness (measured mathematically as the ratio of the sum of all sound energy above to the sum of all sound energy below 2000 Hz and as the frequency at which the ratio of the sum of all sound energy above it to the sum of all sound energy below it equals 0.5) than either pain-induced or hunger crying.

Based on discriminate function analysis, the characteristics of the first and second formants and tenseness contributed most to the linear combination that correctly classified 74% of pain-induced cries. However, the amount of misclassification of cries suggested than any discrete differences among the three cries was minimal. Although computer analysis of cries offers a promising research strategy regarding infant pain assessment, its value in a clinical setting remains unclear.

Finally, Craig, McMahon, Morison, and Zaskow (1984) systematically described changes in pain expression in 30 infants ages 2 to 24 months during an immunization injection. From the time the infants entered the immunization room to the time they left the room, their behavior, using a scale that defined levels of vocal action, nonvocal face, nonvocal torso, and nonvocal limbs, was recorded at 5-second intervals. Because of low interrater reliability, several of the measures were not analyzed. Significant age differences based on analysis of variance for the groups 2 to <12 months and 12 to 24 months included more diffuse, spontaneous movement in the younger children and more goal-directed movement in the older children. The older children also showed more anticipatory distress, such as watching the nurse, than younger children, who did not orient toward, protect, or touch the injection site at all. Younger children vocalized more, especially screaming, than older children.

Although this study contributes additional descriptive information to those few studies that have described developmental trends, it suffers from two main weaknesses. The infant pain behavior rating scale had no established validity and yielded low interrater

reliability. Also, while several age groups were probably observed, the children were divided into two categories and the data analyzed by analysis of variance. Although some group differences were identified, developmental trends along the age continuum were not analyzed. Significant developmental differences exist between children 2 and <12 months and 12 to 24 months; results described for either group may not truly represent all the ages within these two categories.

Circumcision. Several researchers have analyzed behavioral responses of newborns to circumcision with and/or without anesthesia. Most of the studies reviewed in this section were presented earlier during discussion of physiological responses to circumcision. The behavioral variables most commonly observed are cry and state. State refers to state of consciousness and is typically measured according to a six-point scale developed by Brazelton (1973). The six states are (1) quiet sleep (non-REM sleep), (2) active sleep (REM sleep), (3) drowsy, (4) alert, (5) active alert, and (6) crying. Other behavioral variables include facial expression, general distress, and movement. Changes in behavior have also been examined using the Brazelton Neonatal Behavioral Assessment Scale (NBAS) (1973), a widely used instrument that consists of 27 behavioral items, 20 reflexes, and the 6 states described above.

In the Williamson and Williamson (1983) study, the duration of cry was significantly longer immediately after injection of the local anesthetic. However, this anesthetized group displayed significantly less crying at the end of the 4-minute postinjection wait period than the control (unanesthetized) group. During the dissection of the

foreskin, clamp on and off, and the 5-minute postoperative period, the control group cried significantly more. Although both physiological and behavioral variables were monitored continuously for a total of 25 minutes, no attempt was made to correlate the changes. From the graphs and other data given, both cry and heart rate did not return to baseline at the end of the 25-minute period, whereas transcutaneous oxygen did. Heart rate and cry differed only during injection of the anesthetic. However, one possible reason for this difference was that heart rate was already elevated from strapping the infant to the restraint board and cleansing the penis with antiseptic solution. The elevated heart rate may have masked any additional changes during injection of the anesthetic.

From the graphs for transcutaneous oxygen, cry, and heart rate, relationships among the variables were obvious. As crying and heart rate increased, blood oxygenation decreased. This pattern is logical; crying causes apnea, and elevated heart rate causes increased oxygen utilization, both of which lower blood oxygenation. Crying, a vigorous physical activity, raises metabolism and thus the heart rate increases to meet the raised metabolic needs.

Holve et al. (1983) also found significant differences in the percent of crying among three groups of infants (DPNB group, saline group, and no injection group), with the DPNB group crying 50% less than the combined controls during the same steps of the circumcision that affected heart rate (clamping procedures but not injection or clamp removal). Each infant was judged as having a "good" (minimal to no crying or signs of distress), "fair" (slightly more agitation), or "poor" (significant agitation and distress) anesthetic effect.

Fourteen of the 15 (93%) subjects in the DPNB group were observed to have good or fair anesthesia. One of the 8 infants in the saline group was rated as having a fair anesthetic effect, and all of the 8 infants in the no injection group were judged to have a poor anesthetic effect.

The authors commented on the differences found between the behavioral and physiological responses to pain. In the unanesthetized infants (saline and no injection groups) crying decreased while heart rate remained elevated during several procedural intervals. The researchers suggested that reduced crying may indicate fatigue or reflect habituation to repeated painful stimuli. Exhaustion may very well play a role, but habituation seems unlikely, particularly in view of their statement that all three groups became more agitated toward the end of the circumcision.

Cry was also a significant variable in the study by Spencer et al. (1990) comparing lidocaine and chloroprocaine for DPNB. Duration of cry was less in all of the DPNB groups as compared to the control group during lateral clamping, probing, and Gomco placement. The chloroprocaine 3-minute wait group had the least crying of all the DPNB groups. All of the chloroprocaine groups cried less during infusion of the anesthetic as compared to the lidocaine group, but the difference was not significant.

In Masciello's (1990) comparison of cry in two anesthetized (DPNB and local anesthetic) groups and a control group, the percentage of crying time was significantly greater in the control group. However, significant differences also occurred between the two anesthetized groups with the local anesthetic group crying less during lateral

clamping, placement of the device, and clamping of the Gomco, findings almost identical with those of heart rate between the two groups.

No analyses were conducted between the changes in physiological measurements and cry. However, from the data given, it is apparent that no infants were crying 5 minutes after the circumcision but that baseline heart rates had not been reached, even though the increases above baseline were small and not significantly different for any of the groups.

In Mudge and Younger's (1989) study comparing a topical anesthetic group to an unanesthetized group, overall mean crying time throughout the circumcision was significantly less in the anesthetized group. The overt generalized response of the infants, based on subjective impressions by the researchers and physicians regarding facial expression, body movement, and intensity of cry, were reported. Responses were classified as "distressed" and "not distressed." Significant differences were found between the two groups, with only 3 out of 20 infants in the anesthetized group were identified as "distressed," compared to 20 out of 24 in the control group.

No attempt was made to correlate physiological and behavioral responses. However, from the graphs presented, heart rate, respiratory rate, and oxygen saturation did not return to baseline by the end of the circumcision. From the data on overt generalized responses, those infants categorized as "not distressed" probably ceased crying.

In Marchette's and colleagues' two studies comparing the effects of various comfort measures on infants' responses during unanesthetized circumcision, crying occurred during almost all of the

circumcision steps and no comfort group cried significantly less than the control group. The three pacifier groups cried less than the other groups, and the difference may have been significant if number of seconds had been recorded as was done in most other studies. Instead, a code was assigned to the steps in which the subjects cried, whether they cried for all or part of the step (Marchette, Main, Redick, Bagg, and Leatherland, 1991). In their earlier study where facial expression was analyzed using Max, the 2 comfort groups and control group had a physical distress face more than any other emotion for all steps in which infants were touched with surgical instruments (Marchette, Main, & Redick, 1989).

Gunnar, Fisch, and Malone (1984) measured crying by determining behavioral state on a 6-point scale and body tension and activity by using a 3-point scale (1 = quiet, 2 = moderate, and 3 = high) during each 30-second interval for 30-minute periods before, during, and after circumcision. Eighteen unanesthetized males were randomly assigned to a pacifier group or a control (no pacifier) group. A researcher stimulated the subjects to suck on the pacifier for the duration of the circumcision.

The pacifier group cried 40% less and had significantly less movement than the control group. Although the pacifier group had less apparent behavioral distress, it did not have lower cortisol levels postcircumcision as compared to the control group. Also, the percent of crying during circumcision did not predict which infants would be aroused or calm after circumcision, but cortisol levels did. Newborns with higher cortisol levels were behaviorally more aroused in the postcircumcision period. However, the finding may have been related

to the type of surgical procedure. More infants in the control group received the modified Gomco procedure which was associated with increased cortisol levels.

This important study is one of the few on infants' responses to pain that analyzed the relationship between behavioral and physiological changes. The authors hypothesized that the lack of a relationship between cry and cortisol levels may have occurred for at least three reasons. First, measuring cortisol levels 30 minutes after the onset of circumcision may have been too early to detect an effect of differences in behavioral distress. This explanation is unlikely, however, because the testing time was sufficient to identify a difference in cortisol levels due to type of surgical procedure.

Second, the stress-reducing effect of a pacifier may have been too slight to result in a decrease in the infant's adrenocortical response. In this study, the infant was encouraged to suck. Sucking is incompatible with crying; therefore, the sucking may have masked the infant's actual physiological state. As Marchette, and colleagues (1991) showed, the use of a pacifier with or without soothing sound was ineffective in reducing physiological responses to circumcision.

Marchette and colleagues' findings also support the third possible reason, that stimuli that calm the infant have little effect on the adrenocortical responses when the stressor involves pain or tissue damage. As Gunnar, Fisch, and Malone (1984) stated, "Nothing that we were doing to help calm the newborn in any way altered the fact the newborn was experiencing an apparently painful procedure that resulted in tissue damage." They emphasized that the infants' response to stressors, such as pain, may not be detected when only

behavioral measures are obtained.

In another study, sleep states were correlated with changes in plasma cortisol following unanesthetized circumcision in 90 newborns. The subjects were observed at 30-minute intervals before (baseline), during, or after the circumcision, and for 30 minutes before taking the second cortisol sample which occurred at either 30, 90, 120, 150, or 240 minutes from the start of the circumcision. During all observations, a 6-point behavioral state scale was used, with the predominant state being recorded every 30 seconds.

For the 30-minute group, significant changes from baseline occurred in all states, with sleep states decreasing significantly and awake states, except drowsy, increasing significantly. In all the other time-point groups, for the 30-minute observation period before the cortisol sample was taken, active sleep decreased significantly and quiet sleep increased significantly. The greatest increase in quiet sleep occurred between 90 and 120 minutes, when the greatest reduction in cortisol levels was found. The authors suggested that there may be a link between quiet sleep, which is thought to serve as a physiological recovery state, and the reestablishment of baseline cortisol levels (Gunnar, Malone, Vance, & Fisch, 1985).

Stang, Gunnar, Snelman, Condon, and Kestenbaum (1988) compared percent of crying and modal state (based on the six-point scale used in their other studies) in three groups of infants circumcised with lidocaine DPNB, saline injection, or without an injection. The behavioral variables were measured every 30 seconds for 30-minute intervals before, during, and after circumcision. Percent of crying time did not differ for the groups during the injection phase of the

circumcision, suggesting that the DPNB did not increase the infants' distress. This finding differs from that of Williamson and Williamson (1983) but may be due to the different categorization of steps in the procedure. Unlike Williamson and Williamson who analyzed each 30-second interval and found an increase for the first minute but not at the end of the next 4 minutes, these authors averaged the data for the entire 5-minute injection period.

As in all other studies comparing the effectiveness of DPNB, infants in the lidocaine group cried significantly less (23%) of the time during circumcision than the saline group (68%) and the no injection group (71%). The modal state during circumcision was active sleep for the lidocaine group and crying for the 2 control groups. No analysis was performed between the behavioral variables and the change in cortisol levels.

Crying was used to measure the effectiveness of a sucrose-coated pacifier in unanesthetized infants during circumcision (Blass & Hoffmeyer, 1991). Thirty infants were randomly assigned to three conditions: (1) no intervention, (2) a nipple dipped in water, or (3) a nipple dipped in a 24% sucrose solution. A gauze pad placed inside the nipple pacifier was moistened with either solution before and during the Gomco clamp circumcision. Statistically significant differences in percentage of time spent crying occurred. The sucrose-pacifier group cried 31% of the time, compared to 49% in the water-pacifier group and 67% of the time in the no-pacifier group.

In the same report, the results of giving a sucrose or water solution (without pacifier) to newborns ($\underline{N}$ = 24) during heel lancing also showed significantly less crying (42% vs 80%) in the sucrose

group. Based on these findings and those performed earlier in rats, the authors concluded that sucrose has analgesic properties that are probably related to the endogenous opioid system.

In an editorial subsequently published in another journal, the author (unnamed) stated, "Although these observations beg further explanation, Blass and Hoffmeyer's conclusion, based on the assumption that crying denotes pain and that no crying indicates effective analgesia, is highly contentious" (Editorial, 1992). This study typifies the potentially false conclusions that can be reached when only one measure of pain is used. As Gunnar, Fisch, & Malone (1984) showed, crying decreased with the use of a pacifier but cortisol levels remain elevated, indicating physiological distress from the circumcision. Field and Goldson (1984) also found that the use of a pacifier decreased crying in sick premature infants during a heel lance, but that the subjects' heart rates remained elevated.

Researchers have suggested that sucking on a pacifier reduces crying because the two activities are incompatible. Blass and Hoffmeyer addressed this possibility but believed that the results of the heel lance study provided evidence for sucrose's independent analgesic effect. Again, the use of only one measure, crying, can be misleading because this behavior is not specific for pain. Infants also cry because they are hungry. The small amount of sucrose may have temporarily minimized the hunger, having a pacifying effect unrelated to analgesia.

With only cry used to assess the effectiveness of sucrose in alleviating pain, the results of this study are highly questionable. This is unfortunate because there are no data to disprove the analgesic

benefits of sucrose. In fact, Blass and Fitzgerald (1988) have published intriguing results on the effectiveness of milk to decrease distress vocalization in 10-day old rats. The most impressive finding was that naltrexone, an opioid antagonist, reversed the analgesia induced by the milk.

From this review of studies that used cry as an indicator of pain, it is evident that cry is a consistent response to a noxious stimuli, but not necessarily a specific one. Infants may also cry from other disturbing events, such as restraint, that are not nearly as painful as circumcision. Probably the most important finding about using cry to assess pain is its relationship to physiological variables, such as heart rate and cortisol. Crying typically subsided before heart rate and cortisol levels return to baseline, which can erroneously imply that the infant is physiologically recovered.

Marshall, Stratton, Moore, and Boxerman (1980) analyzed behavioral changes using the NBAS in 14 newborns circumcised without anesthesia at 2 days of age (early group). A control (delayed) group of 12 infants was circumcised at 3 weeks of age, allowing for the same four NBAS examination times (2 on day 2, 1 on day 3, and 1 at 3 weeks of age). Results were only presented for the first three examinations.

In a preliminary analysis of the differences between the two NBAS scores obtained at day two (for the circumcision group, the testing was performed before and after the surgery; for the delayed group the testing was done at the same times), no significant differences were found. However, both physician investigators correctly identified about 85% of the subjects' circumcision status, indicating that

differences in behavior had occurred but were not detected by the usual NBAS scoring method. Therefore, a reduction scale was developed which organized 10 NBAS items into three distinct clinical behavior categories - average, subdued, or hyperactive.

In the early circumcision group 12 of 14 (87%) infants changed behavior categories on day 2, a significant difference from only 2 of 12 (16%) infants in the delayed group. When examined at day 3 (22 hours after the circumcision), two-thirds of the circumcised subjects who had changed behavior categories reverted back to their initial category. However, the other third showed persistence of the behavior changes found immediately after the surgery.

The direction of the behavior changes after circumcision was diverse. Seven of 12 (58%) infants became more active and 5 of 12 (42%) became less active. The only difference observed between these two groups was their precircumcision state. Most of the subjects who became more active postcircumcision (83%) were crying precircumcision, whereas 80% of the infants who became less active postcircumcision were in the quiet alert state precircumcision.

In a study by Dixon, Snyder, Holve, and Bromberger (1984) behavioral changes as demonstrated by the NBAS were compared in three groups of infants just before and after circumcision and on the day following the procedure. One group (n = 15) received a DPNB, another group (n = 8) received a saline injection simulating a DPNB, and the final group (n = 8) received no injection. NBAS examinations were performed on 16 infants selected randomly from the three circumcision groups.

Total mean scores of the NBAS for the three groups could not be

compared in any meaningful way. However, the examiners correctly identified 71% of the subjects' group assignment. They perceived the saline and no injection infants to be more irritable or more somnolent, requiring more effort to bring forth the subjects' best performance and being less available for social interaction.

When the individual items or cluster of items on the NBAS were compared among the groups, significant differences were found. In comparing scores on the pre- and postcircumcision examinations, the researchers found more optimal performances in the DPNB group for orientation (attention to animate and inanimate objects), motor processes (smoothness and maturity of movement), and habituation (ability to "tune out" stimuli).

When the scores from the precircumcision testing were compared to the day-after circumcision testing, the same findings regarding the orientation and motor clusters were found. In addition, the DPNB group scored significantly better on the self-quieting item (more able to quiet self after distress) and on irritability (less irritable). This study provided further evidence that circumcision without anesthesia significantly affected the infants' behavior both immediately and up to one day after the procedure.

Other Painful Procedures. Three studies are reviewed separately because each assessed infants' responses to deliberately inflicted pain or to pain during a variety of procedures. The first study is the most extensive investigation on the developmental responses of children to pain. McGraw (1941) used a pinprick as a stimulus (ten pricks in each of the following areas: head, trunk, upper and lower extremities) and recorded either on motion picture film or by written

protocols 2008 observations on 75 children from birth to 4 years of age. In addition to these serial records over a period of years, daily observations were kept on 4 infants during the first 18 to 24 months of age.

Four sensori-motor phases were identified to describe the infants' behaviors. In the newborn or diffuse phase, some infants only a few hours or days old exhibited no overt response. However, by 7 to 10 days most infants reacted to cutaneous irritation with diffuse bodily movements accompanied by crying and possibly a local reflex withdrawal of the stimulated extremity. The inhibitive phase (low response) began with the reaction increasing in intensity during the first month, but beginning to decline during the second month. The lowest response occurred at about 4 months. In the general localization phase, infants ages 6 to 12 months exhibited deliberate, rather than reflexive, withdrawal of the stimulated limb. The withdrawal was often preceded by visual fixation on the point of stimulation. In the specific localization phase which began toward the end of the first year, infants touched the pricked area after the stimulus was withdrawn. Later the children anticipated the application of the stimulus and tried to actively push it away.

McGraw also described the cognitive phases of the infants' behavior, which generally lagged behind that of the sensori-motor responses. In the passive or newborn phase and for some time thereafter, infants demonstrated no detectable response to the approaching pin. In the object perception phase which roughly began at about 3 months of age, infants looked at the pin, grasped it, and played with it like any other item. There was no evidence that the

pin was associated with the forthcoming discomfort. During the associative phase which appeared at about 6 months, infants demonstrated awareness of the pin's purpose by fussing, crying, or withdrawing. In the latter part of this phase the children could state their demands, such as "No pin" or "Don't stick me," or actively pushed the stimulus away. The integrative phase which encompassed most children by 26 months of age was characterized by awareness of the forthcoming stimulus and aggressive, often effective, attempts to prevent the pinprick.

With the exception of the newborn period, subsequent research has supported McGraw's findings (Craig, McMahon, Morison, & Zaskow, 1984; Dale, 1986; Mills, 1989). However, other researchers have found that all newborns reacted to a heel puncture by immediate withdrawal of both the affected and unaffected leg, movement of other extremities, facial grimacing (Franck, 1986), and increases in heart rate (Owens & Todt, 1984). Reasons for the discrepancy in findings might include the use of different noxious stimuli, measurement of different responses, and within-subjects variability. The likelihood of the pinprick versus the heel lance contributing to the difference is logical, in that the pinprick induces less pain than an actual skin puncture. However, this difference is not supported by Owens' and Todt's findings that newborns reacted to the less noxious stimulation of restraining and rubbing the heel with alcohol, although less intensely than the actual heel puncture. More substantiated reasons are that McGraw's reliance on only one observation, gross motor responses, led to the conclusion of no reaction, when in fact heart rate could have been increased or subtle movements could have occurred

which were not measured. Also, state is an important variable to consider; the infant's state at the time of applying the stimulus affects the intensity of the response (Grunau & Craig, 1987). The state of McGraw's subjects was not addressed.

Mills (1989) described the behaviors of 32 hospitalized children ages 0 to 36 months following surgery, fractures, or burns. The purpose of the study was to determine the relationship between age and pain behaviors that were clustered into three categories: motor movement, communication, and facial expression. She found a development trend in each category. For motor movement, the trend was from general body movement (wiggling, kicking, flailing, and so on) to purposeful movements (pulling away, pushing nurse's hand away, rubbing body part, and so on). Communication also changed from crying after the inflicted pain to anticipatory crying and verbal reports of pain. Facial expressions were described as frowns, grimaces, and clenched jaw in the youngest infants to pouting in the oldest children. Although this study did not provide much new information on the relative merits of these three behavior categories for assessing acute pain, it is one of the few recent investigations that provided data regarding developmental trends. Her findings with respect to movement and vocalizations are very similar to those of McGraw.

Finally, Davis and Calhoon (1989) examined whether sick premature infants ($\underline{N}$ = 12) exhibited behavioral responses to painful procedures (chest physiotherapy, venipunctures, suctioning, and electrode and dressing changes) that differed from their behaviors during routine care (feeding, changing diapers, and measuring vital signs). Ten infant behaviors were examined: four sleep/wake states, negative

facial expression (cry face or frown), jitter, startle, hiccup, spit-up or gag, and gross motor movement. The results showed that during painful care as opposed to routine care the percentage of waking was significantly greater (34.4% vs 17.0% respectively), while active sleep (32.8% vs 56.6%) and quiet sleep (9% vs 2.4%) occurred less. The only other behaviors that were significantly more frequent during painful care were negative facial expressions (38.9% vs 17.4%) and gross movement (69.2% vs 45.4%). These findings support the view that infants as young as 29 weeks gestational age exhibit behavioral responses to painful procedures that differ from responses to routine care, and provide additional evidence for the validity of state, facial expression, and cry as pain indices.

Results of Efforts to Control Pain in Infants

Despite the burgeoning number of studies investigating infants' responses to pain, very few studies have addressed the seminal question of whether treating pain is beneficial to infants. Rather, the predominant view among health professionals has been that pain is less detrimental than its treatment, especially in regard to the risk of opioid-induced respiratory depression. In fact, in Schechter and Allen's (1986) survey of physicians, 63% stated that concern about respiratory depression somewhat (42%) or always (21%) limited their prescribing opioids for pain.

The classic studies of Anand and his colleagues on the use of different types of anesthesia during surgery of newborns offer the only evidence of the outcomes of adequate pain control. In the

studies comparing "light" anesthesia (nitrous oxide and curare) to "deep" anesthesia (either fentanyl or halothane), the infants receiving deep anesthesia had significantly fewer postoperative complications (Anand, Sippell, & Aynsley-Green, 1987; Anand, Sippell, Schofield, & Aynsley-Green, 1988). In a third study comparing types of anesthesia and postoperative analgesia, the group receiving more intense pain control not only had significantly less postoperative morbidity, but also significantly lower mortality (no deaths in the group of 30 infants who received more intense analgesia, compared to 4 deaths in the group of 15 infants who received less intense analgesia) (Anand & Hickey, 1992). These important studies not only demonstrate the beneficial effects of deep anesthesia and/or postoperative analgesia in reducing the stress response, but also that the magnitude of the stress response can influence the body's ability to recover.

Although no formal studies were found to support this contention, some practitioners suggest that pain control may be important in reducing the risk of intraventricular hemorrhage (IVH) in critically ill infants. Of the physiological mechanisms involved in the development of IVH, increased blood pressure is thought to be a key factor in increasing intracranial bloodflow, intracranial pressure, and rupture of fragile blood vessels (Perry et al., 1990). Pain induces an autonomic stress response that significantly elevates blood pressure. One anecdotal report of an institution's attempt to reduce the risk of IVH included the increased use of analgesics in critically ill newborns (Philip, Allan, Tito, & Wheeler, 1989).

Three thought-provoking reports suggest that early experiences may have long lasting, detrimental effects. Two studies analyzed

perinatal factors to determine if they increased the risk of suicide. Jacobson et al. (1987) investigated the birth records of 412 Swedish victims who were born between 1940 and 1965 and died between 1978 and 1984) from suicide, alcoholism, or drug addiction. Their birth data were compared to a control of 290 other birth records.

The results showed that the type of suicide was significantly related to the type of birth trauma. Suicide by asphyxiation (hanging, strangulation, drowning, and inhalation poisoning) was four times more likely to be associated with asphyxia during birth, than for the controls. Suicide by mechanical injury (hanging, strangulation, jumping from heights, and firearms) was twice as likely to be associated with mechanical birth trauma (breech presentation, forceps delivery, umbilical cord around the neck) than for the controls. Drug addict victims were much more likely to have been born to mothers who received opiates (two times more) and barbiturates (three times more) than the controls.

The authors hypothesized that this association between birth events and death by self-destruction may be related to imprinting, which creates an unconscious need to repeat traumatic experiences at birth as an adult. They added that regardless of what mechanism may transfer the trauma from birth to adulthood, the birth experience should be carefully evaluated and possibly modified to prevent eventual self-destructive behavior.

In a similar study Salk, Lipsitt, Sturner, Reilly, and Levat (1985) analyzed the perinatal records of 52 adolescents in the United States who committed suicide before age 20 and two matched controls for each victim. The results showed three perinatal risk factors for

the adolescent suicides (1) respiratory distress for more than one hour at birth, (2) no perinatal care before 20 weeks of pregnancy, and (3) chronic disease of the mother during pregnancy. These three factors occurred alone in 81% of the suicide cases, in combination with one other factor in 19%, and never in combination with two other factors. Therefore these variables operated fairly independently of one another.

The authors suggested that there is a relationship between the increasing suicide rate in adolescents and the decreasing perinatal mortality rate over the last three decades. They did not suggest a direct relationship but some interplay of factors that make individuals with stressful early life experiences more vulnerable to self destruction in later life. The finding of early respiratory distress in this study and birth asphyxia in the Swedish study is intriguing. Not only may the lack of oxygen somehow have affected neurological functioning in these newborns, but it is also plausible that treatment for the respiratory problems exerted an influence. Suctioning, awake intubation, and all the diagnostic procedures, such as arterial or heel punctures, that are part of the treatment, are painful.

Laboratory experiments with animals show that pleasure and violence have a reciprocal relationship -- the presence of one inhibits the other. When the brain's pleasure circuits are "on," the violence circuits are "off" and vice versa (Mitchell, 1975). Extending these findings to humans, Rice (1985) hypothesized that early sensory experiences during fetal and infant development may create a neuropsychological predisposition for either violence-seeking

or pleasure-seeking behaviors later in life. Rice suggested that perinatal violence, such as a stressful intrauterine environment, traumatic birth, early mother-infant separation, and pain can influence the predisposition for violence seeking behavior.

While such a theory has yet to be proven, the findings of aversion to human touch in infants experiencing prolonged stays in intensive care units as discussed in the section on Memory of pain lends support to such contentions. Also, preliminary research on the effects of early experience on neural development in animals cannot be ignored.

Greenough, Black, and Wallace (1987) have proposed two theoretical processes that may account for the way the infant's brain may be affected by experience. In this scheme, experience expectant information refers to the incorporation of environmental information that is ubiquitous in the environment and common to all species members. An important component of the neural processes underlying experience-expectant information storage appears to be the intrinsically governed generation of an excess of synaptic connections among neurons. Additional experiential input subsequently determines which of the synaptic connections survive.

The second process is experience dependent, which involves storage of information that is unique to the individual. An important aspect of the mechanism underlying experience-dependent information storage appears to be the generation of new synaptic connections. Pain can be viewed as both information that is common to all infants and as information that is unique to the individual. Therefore, it is plausible that additional painful experiences will in some way affect

brain development.

Research on animals has provided support for the "experience dependent" process. Using Pavlovian conditioning, researchers trained rabbits to blink every time a bell was rung by pairing the bell with a mild puff of air directed into one eye. The rabbits' brains were then examined for the number of synaptic connections in the specific areas of the cerebellum that controlled the eyeblink behavior. The researchers found a significant difference in the number of synaptic connections on either side of the cerebellum; the side trained to blink had more synaptic connections (Greenough & Anderson, 1991). The researchers noted that the brain has the potential for trillions of such neural connections, so that the physical structure of the brain does not limit the number of experiences that can be remembered.

Another study showed that early handling of neonatal rats affected hippocampal development by increasing the number of hippocampal glucocorticoid receptors. Rats not handled secreted more glucocorticoid in response to stress and had greater hippocampal cell loss at later ages. The researchers suggested that prolonged exposure to higher levels of glucocorticoid results in death of specific neurons (Meaney, Aitken, Van Berkel, Bhatnager, & Sapolsky, 1988).

The Present Study

While the body of knowledge on pain assessment in infants has undergone unprecedented growth during the last decade, several issues require additional investigation or remain unanswered. One aim of the present study, the first research question, is to examine the

physiological (heart rate and oxygen saturation) and behavioral (cry and facial expression) changes that occur in infants in response to an injection.

Analysis of heart rate has been limited to reports of the absolute or percent changes for the entire sample that almost exclusively focused on newborns. There is a need to study older infants and take finer-grained measurements, such as time to maximum heart rate and differences in heart rate changes among age groups, and to explore developmental trends.

Although a few investigations have analyzed fluctuations in oxygen saturation, none has analyzed the changes in response to pain in infants beyond the perinatal period. Of the few studies reporting saturation changes, one found that in premature infants oxygen saturation returned to baseline after heart rate and intracranial pressure (Stevens, 1991). However, premature infants may not represent the norm. Also, there is a need to measure oxygen saturation using the instrumentation that minimizes interference from movement, a critical factor in obtaining valid measurements.

Cry has been used as a behavioral index of pain in numerous studies, which have included detailed and complex acoustical analysis. However, few studies have examined cry along a developmental continuum, in relation to physiological measures, and as a measure of soothing.

Significant work has been done on systematically coding facial expressions in relation to pain. Although there is no consensus on the relative merits of coding instruments, such as the Neonatal Facial Coding System or the Max, both describe an almost identical pain

expression. However, only the Max has a theoretical basis. Certainly, in terms of child development, one critical assumption of differential emotions theory is that change in facial expression is a function of maturation, rather than experience. This study will attempt to address that assumption across several age groups, using both regression analysis and analysis of variance to identify trends.

A second research question addresses the relationship between the physiological and behavioral responses, an issue that has been reported in very few studies. Since discussions about treating pain are often based on the child's outward distress, it is critical to know if behavioral upset, such as crying, is a valid indicator of the total stress being experienced. Based on the limited evidence to date with infant subjects, it appears that behavior can be misleading, especially if used as the only pain index. When the cortisol levels and behavioral responses of infant monkeys were monitored before, during, and after separation from their mothers and placement with surrogate monkeys, they demonstrated cortisol elevations usually observed following separation and placement in a solitary cage, but showed none of the usual protest behaviors (Levine, 1982).

Of all of the research done on infant pain, none has considered the effect of prior painful experiences on infants' present responses to pain. The third research question is concerned with this unexplored and important issue that is critical to a fuller understanding of the role that pain history can have on very young children's physiological and behavioral responses to present pain.

This question may also provide evidence relating to infants' memory of pain, which many health professionals contend does not exist

and consequently, does not justify being treated. If prior experiences influence current pain responses, pain experiences may be mentally stored and affect future psychobiological function.

Although the study of the psychobiology of stress in infants is in its own infancy, preliminary research seems to suggest a relationship between heightened reactivity to environmental stressors, such as pain, and greater risk for both acute and long-term alterations in health. For example, 2-month-old infants with more intense responses of cry and facial expression to an immunization injection were more likely to have a history of atopy and infectious illnesses by 2 years of age, than infants with a less intense response (Lewis, Thomas, & Worobey, 1990).

The ultimate goal of this study is to change clinical practices that currently fail to relieve pain adequately. If a person's pain is to be treated, it must be recognized by others. If pain cannot be clearly communicated, it remains an isolated experience, easily ignored, or misinterpreted (Shapiro & Ferrell, 1992). The findings from this research may add to the existing body of knowledge of infant pain, making it more possible to alleviate needless suffering.

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APPENDIX B

NOMENCLATURE

NOMENCLATURE

after bandaid	30-second interval beginning after applying bandaid (for analysis of facial expressions)
anger expression	facial expression same as physical distress expression except eyes kept opened
ANOVA	analysis of variance
baseline heart rate	mean of two apical heart rates measured with stethoscope in waiting room and in examination room before any monitoring equipment placed on subject; if only second heart rate taken, this value used as baseline
before bandaid	interval ending at time of applying bandaid (for analysis of facial expressions)
DPNB	dorsal penile nerve block
DTP	diphtheria, tetanus, pertussis
ECG	electrocardiocardiography
Hib	Haemophilus influenzae type B
in time	time in seconds from needle piercing skin; zero point for all time measurements used for data analysis
IPI	Infant Pain Inventory
Max	Maximally Discriminative Facial Movement Coding System
maximum fractional increase in heart rate $(R_{max} - R_o)/R_o$	maximum heart rate minus baseline heart rate divided by baseline heart rate or, if decimal value multiplied by 100, percent increase in baseline heart rate
MFIIPR	maximum fractional increase in pulse (heart) rate
MMR	measles, mumps, rubella
NBAS	Neonatal Behavioral Assessment Scale
normalized heart rate	instantaneous heart rate at given point in rate time divided by baseline heart rate, or ratio of instantaneous heart rate to baseline heart rate

physical distress	facial expression of lowered brows expression drawn together; bulging, vertical furrows in forehead between brows; broadened and bulging nasal root; fissured, tightly closed eyes; and angular, squarish mouth
predominant physical distress or anger	proportion of children demonstrating either facial expression for more than 50% but less than 100% of time
pulse soothing	heart rate returned to baseline within 3 minutes
R-DDST	Revised-Denver Developmental Screening Test
(Rmax - Ro)/Ro	maximum fractional increase in heart rate
R-PDQ	Revised Denver Prescreening Developmental Questionnaire
soothing or behavioral soothing	cessation of crying for at least 10-second interval followed by no return of extended crying within 3 minutes
soothing time	time until behavioral soothing occurred
Tic	time to first audible cry
time to initial cry	time to first audible cry
time to maximum heart rate (Trmax)	time to reach maximum heart rate
time to pulse soothing (Tps)	time until heart rate returned to baseline within 3 minutes
Trmax	time to reach maximum heart rate
total pain score	sum of number of painful events reported by parent that child experienced from birth to before participating in study
total physical distress or anger	proportion of children demonstrating either facial expression 100% of time
Tps	time to pulse soothing
Trmax	time to reach maximum heart rate
Ts	time to behavioral soothing

APPENDIX C

INSTRUMENTS

0-9 MONTHS
(R-PDQ)

REVISED DENVER PRESCREENING DEVELOPMENTAL QUESTIONNAIRE

Child's Name _____

Person Completing R-PDQ: _____

Relation to Child: _____

CONTINUE ANSWERING UNTIL **3 "NOs"** ARE CIRCLED

For Office Use

1. Equal Movements
When your baby is lying on his/her back, can (s)he move each of his/her arms as easily as the other and each of the legs as easily as the other? Answer **No** if your child makes jerky or uncoordinated movements with one or both of his/her arms or legs.

Yes **No** (0) FMA

2. Stomach Lifts Head
When your baby is on his/her stomach on a flat surface, can (s)he lift his/her head off the surface?

Yes **No** (0-3) GM

3. Regards Face
When your baby is lying on his/her back, can (s)he look at you and watch your face?

Yes **No** (1) PS

4. Follows To Midline
When your child is on his/her back, can (s)he follow your movement by turning his/her head from one side to facing directly forward?

Yes **No** (1-1) FMA

5. Responds To Bell
Does your child respond with eye movements, change in breathing or other change in activity to a bell or rattle sounded outside his/her line of vision?

Yes **No** (1-2) L

6. Vocalizes Not Crying
Does your child make sounds other than crying, such as gurgling, cooing, or babbling?

Yes **No** (1-3) L

7. Smiles Responsively
When you smile and talk to your baby, does (s)he smile back at you?

Yes **No** (1-3) PS

For Office Use

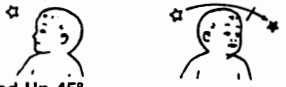
Today's Date: ____ yr ____ mo ____ day

Child's Birthdate: ____ yr ____ mo ____ day

Subtract to get Child's Exact Age: ____ yr ____ mo ____ day

R-PDQ Age: (____ yr ____ mo ____ completed wks)

8. Follows Past Midline
When your child is on his/her back, does (s)he follow your movement by turning his/her head from one side ***almost all the way to the other side?***



Yes **No** (2-2) FMA

9. Stomach, Head Up 45°
When your baby is on his/her stomach on a flat surface, can (s)he lift his/her head 45°?

Yes **No** (2-2) GM

10. Stomach, Head Up 90°
When your baby is on his/her stomach on a flat surface, can (s)he lift his/her head 90°?

Yes **No** (3) GM

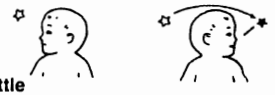
11. Laughs
Does your baby laugh out loud without being tickled or touched?

Yes **No** (3-1) L

12. Hands Together
Does your baby play with his/her hands by touching them together?

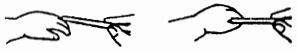
Yes **No** (3-3) FMA

13. Follows 180°
When your child is on his/her back, does (s)he follow your movement from one side ***all the way*** to the other side?



Yes **No** (4) FMA

14. Grasps Rattle
It is important that you follow instructions carefully. Do ***not*** place the pencil in the palm of your child's hand. When you touch the pencil to the back or tips of your baby's fingers, does your baby grasp the pencil for a few seconds?



TRY THIS NOT THIS

Yes **No** (4) FMA

(Please turn page)

CONTINUE ANSWERING UNTIL 3 "NOs" ARE CIRCLED

15. Sits, Head Steady
When sitting, can your child hold his/her head upright and steady? Answer **No** if his/her head falls to either side or upon his/her chest.

Yes **No** (4) GM

16. Stomach Chest Up-Arm Support
When your baby is on his/her stomach on a flat surface, can (s)he lift his/her chest using his/her arms for support?

Yes **No** (4-1) GM

17. Squeals
Does your baby make happy high-pitched squealing sounds which are not crying?

Yes **No** (4-2) L

18. Rolls Over
Has your baby rolled over at least 2 times, from stomach to back, or back to stomach?

Yes **No** (4-3) GM

19. Regards Raisin
Can your child focus his/her eyes on small objects the size of a pea, a raisin, or a penny?

Yes **No** (5) FMA

20. Reaches For Object
Can your child pick up a toy if it is placed within his/her reach?

Yes **No** (5) FMA

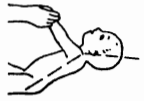
21. Smiles Spontaneously
Does your child smile at crib toys, pictures, or pets when (s)he is playing by himself/herself?

Yes **No** (5) PS

22. Pull To Sit, No Headlag
With your baby on his/her back, gently pull him/her up to a sitting position by his/her wrists. Does your baby hold his/her neck stiffly like the baby in the picture below left? Answer **No** if his/her head falls back like the baby in the picture below right.

Yes **No** (6-1) GM

Yes



No

For Office Use

Side #2

23. Sits, Looks For Yarn
Please follow directions carefully. Get your baby's attention with a scarf, handkerchief, or a tissue and then drop it ***out of sight.*** Did your baby try to find it? For example, did (s)he look for it under the table or continue to watch where it disappeared?

Yes **No** (7-2) FMA

24. Passes Cube Hand To Hand
Can your baby pass something, such as a small block or a small cookie, from one hand to the other? Long objects like a spoon or rattle do not count.

Yes **No** (7-2) FMA

25. Sits, Takes 2 Cubes
Can your baby pick up 2 things, such as toys or cookies, and hold one in each hand at the same time?

Yes **No** (7-2) FMA

26. Bears Some Weight On Legs
When you hold your baby under his/her arms, can (s)he bear some weight on his/her legs? Answer **Yes** only if (s)he tries to stand on his/her feet and supports some of his/her own weight.

Yes **No** (7-3) GM

27. Rakes Raisin, Attains
Can your baby pick up small objects, such as raisins or pieces of food with his/her hand using a raking or grabbing motion?

Yes **No** (7-3) FMA

28. Sits Without Support
Without being propped by pillows, a chair, or wall, can your child sit by himself/herself for 60 seconds?

Yes **No** (7-3) GM

29. Feed Self Crackers
Can your baby feed himself/herself a cracker or cookie? Answer **No** if (s)he has never been given one.

Yes **No** (8) PS

30. Turns To Voice
When your child is playing and you come up ***quietly*** behind him/her, does (s)he sometimes turn his/her head as though (s)he heard you? ***Loud sounds do not count.***

Yes **No** (8-1) L

9-24 MONTHS (R-PDQ)

REVISED DENVER PRESCREENING DEVELOPMENTAL QUESTIONNAIRE

Child's Name _____

Person Completing R-PDQ: _____

Relation to Child: _____

For Office Use

Today's Date: ____ yr ____ mo ____ day

Child's Birthdate: ____ yr ____ mo ____ day

Subtract to get Child's Exact Age: ____ yr ____ mo ____ day

R-PDQ Age: (____ yr ____ mo ____ completed wks)

CONTINUE ANSWERING UNTIL **3 "NOs"** ARE CIRCLED

29. Feed Self Crackers
Can your baby feed himself/herself a cracker or cookie? Answer **No** if (s)he has never been given one.
Yes **No** (8) PS

30. Turns To Voice
When your child is playing and you come up quietly behind him/her, does he/she sometimes turn his/her head as though (s)he heard you? ***Loud sounds do not count.***
Yes **No** (8-1) L

31. Works For Toy Out Of Reach
When a desired toy is out of easy reach, does your baby try to get it by stretching his/her arms or body?
Yes **No** (9) PS

32. Plays Peek-A-Boo
When you hide behind something (or around a corner) and reappear again and again, does your baby look for you or eagerly wait for you to reappear?
Yes **No** (9-3) PS

33. Dada Or Mama, Nonspecific
Does your baby make either "ma-ma" or "da-da" sounds?
Yes **No** (10) L

34. Pulls Self To Stand
Can your baby pull himself/herself to a standing position without help?
Yes **No** (10) GM

35. Resists Toy Pull
Give your baby a pen or pencil. You may place it in the palm of his/her hand. Gently try to pull it away from him/her. Is it difficult for you to get the pen or pencil back?
Yes **No** (10) PS

36. Stands Holding On
Can your baby stand holding on to a chair or table for ***30 seconds*** or more?
Yes **No** (10) GM

37. Initially Shy With Strangers
Can your child tell you from strangers? (S)He may show this by at first being a little shy or hesitant with strangers.
Yes **No** (10) PS

38. Thumb-Finger Grasp
When your baby picks up a small object, such as a raisin, does (s)he do so by squeezing it between his/her thumb and fingers?
Yes **No** (10-1) FMA

For Office Use

39. Gets To Sitting
Can your baby get to a sitting position without help?
Yes **No** (11) GM

40. Imitates Speech Sounds
Write down 2 or 3 words that your baby tries to imitate with a recognizable sound (not necessarily complete words).

In your judgment, does (s)he try to imitate words?
Yes **No** (11) L

41. Bangs 2 Cubes Held In Hands
Without your moving his/her hands, can your baby bang together 2 small blocks? Rattles and pan lids do not count.
Yes **No** (12-1) FMA

42. Walks Holding On Furniture
Can your baby walk alone or walk holding on to furniture?
Yes **No** (12-3) GM

43. Stands Momentarily
Can your baby stand alone without having to hold on to something for about ***5 seconds?***
Yes **No** (13) GM

44. Plays Pat-A-Cake
Can your baby play "pat-a-cake" or wave "bye-bye" without help? Answer **No** if you need to help him/her by holding his/her hands.
Yes **No** (13) PS

45. Dada or Mama, Specific
Does your child say "da-da" when (s)he wants or sees his/her father? Does your child say "ma-ma" when (s)he wants or sees his/her mother? Answer **Yes** if your child says ***either.***
Yes **No** (13-1) L

46. Stands Alone Well
Can your baby stand alone without having to hold on to something for ***30 seconds*** or more?
Yes **No** (13-3) GM

47. Stoops And Recovers
Without holding on to something or touching the floor, can your child bend over to pick up a toy or other object on the floor and stand up again?
Yes **No** (14-1) GM

(Please turn page)

CONTINUE ANSWERING UNTIL 3 **"NOs"** ARE CIRCLED

48. Indicates Wants (Not Cry)
Can your child indicate what (s)he wants without crying or whining? (S)He may do this by pointing, pulling, or making pleasant sounds.

Yes **No** (14-1) PS

49. Walks Well
Can your child walk all the way across a large room without falling or wobbling from side to side?

Yes **No** (14-1) GM

50. Neat Pincer Grasp Of Raisin
Can your baby pick up a small object, such as a raisin, using only his/her thumb and index finger?

Yes **No** (14-3) FMA

51. Plays Ball With Examiner
If you roll a ball to your child, can (s)he roll or throw it back towards you? Answer **No** if your child only hands the ball to you, or if you have never tried this.

Yes **No** (16) PS

52. Drinks From Cup
Can your child hold a regular cup or glass by himself/herself and drink from it without spilling? The cup should not have a spout.

Yes **No** (16-2) PS

53. Imitates Housework
When you are doing housework, does your child copy what you are doing?

Yes **No** (19-2) PS

54. Tower Of 2 Cubes
Can your child put a block on top of another without the block falling? This applies to ***small*** blocks about 1 inch in size and not blocks more than 2 inches in size.

Yes **No** (20) FMA

55. 3 Words Other Than Mama, Dada
Can your child say at least ***3*** specific words, other than "da-da" and "ma-ma," which mean the same thing each time (s)he uses them?

Yes **No** (20-2) L

For Office Use

Side #2

56. Walks Backward
Can your child take ***5*** or more steps backwards without losing his/her balance? You may have seen him/her do this while pulling a toy.

Yes **No** (21-2) GM

57. Removes Garment
Can your child take off any of his/her clothes, such as pajamas (tops or bottoms) or pants? Diapers, hats and socks do not count.

Yes **No** (21-3) PS

58. Walks Up Steps
Can your child walk up steps by himself/herself or by holding on to the wall or railing for support? Answer **No** if: 1) (s)he has to crawl up the stairs; 2) you do not let him/her climb stairs; or 3) (s)he has to hold on to a person or the next step.

Yes **No** (22) GM

59. Points To 1 Named Body Part
Without your coaching, pointing, or helping, can your child point to at least 1 part of his/her body (hair, eyes, nose, mouth, or any other part) when asked? Answer **Yes** only if (s)he knows this well enough that (s)he will point when asked by a stranger.

Yes **No** (23) L

60. Uses Spoon, Spilling Little
Can your child feed himself/herself with a spoon or fork without spilling much?

Yes **No** (23-2) PS

61. Helps In House – Simple Tasks
Does your child help pick up his/her toys or help carry the dishes when asked? Answer **Yes** only if (s)he can ***complete*** either of these tasks.

Yes **No** (23-2) PS

For Office Use

CODE:_____ TESTER/DATE:_____

PARENT INTERVIEW

SUBJECT'S NAME:_____

ADDRESS:_____
city___ semi-rural___ rural___

TELEPHONE NO._____

SEX:___ RACE: white___ black___ hispanic___ other (specify)____

BIRTH DATE:_____ VACCINE:_____ MD/NURSE:_____

HOSPITAL DATE(S) (include birth):_____ HOSPITAL:_____

MOTHER'S EDUCATION: number of school years completed _____

PAINFUL PROCEDURES/EVENTS
Prenatal to Birth

Pain Item (Code # from IPI)	Pain Rating (0-10)	Quality Rating (0-10)	Comments
1. Amniocentesis			
3. Internal fetal monitoring			
4. Vaginal delivery			
5. Cesarean delivery			
6. Use of forceps			
9. Circumcision (no anesthetic)			
(with anesthetic)			
10. Vitamin K injection			
11. Heel puncture			

Common Postnatal Health Conditions and Injuries

64. Colic			
65. Otitis media			
66. Gastroenteritis			
67. Urinary tract infection			
68. Diaper dermatitis			
69. Teething			
70. Falling			
71. Cuts			
73. Fracture			
74. Electrical shock (minor)			
75. Burns (degree)			

Additional items: (ex. Postnatal Medical Procedures)
.....
.....

I. INFANT PAIN INVENTORY: Prenatal to Birth

Pain Item	Pain Rating (0-10)	Quality Rating (0-10)	Comments
1. Amniocentesis			
2. Fetal blood sampling			
3. Internal fetal monitoring			
4. Vaginal delivery			
5. Cesarean delivery			
6. Use of high forceps			
7. Use of low forceps			
8. Measuring axillary temperature			
9. Circumcision (no anesthetic)			
(with anesthetic)			
10. Vitamin K injection			
11. Heel puncture			
12. Umbilical cord care			
Additional items:			

II. INFANT PAIN INVENTORY: Postnatal Medical Procedures

Pain Item	Pain Rating (0-10)	Quality Rating (0-10)	Comments
13. Intramuscular injection			
14. Intravenous injection			
15. Subcutaneous injection			
16. Intradermal injection			
17. Venipuncture (obtain blood)			
(insert IV)			
18. Arterial puncture (obtain blood)			
(insert arterial line)			
19. Heel puncture			
20. Finger puncture			
21. Removal of intravenous line			
22. Removal of arterial line			
23. Measuring axillary temperature			
24. Measuring rectal temperature			
25. Bone marrow aspiration (without local anesthetic)			
(with local anesthetic)			
26. Bone marrow biopsy (without local anesthetic)			
(with local anesthetic)			
27. Lumbar puncture (without local anesthetic)			
(with local anesthetic)			
28. Chest tube insertion (without local anesthetic)			
(with local anesthetic)			
29. Chest tube removal (without local anesthetic)			
(with local anesthetic)			
30. Laryngoscopy			

INFANT PAIN INVENTORY: Postnatal Medical Procedures, cont.

Pain Item	Pain Rating (0-10)	Quality Rating (0-10)	Comments
31. Insertion of endotracheal tube			
32. Removal of endotracheal tube			
33. Mechanical ventilation			
34. Chest percussion/vibration			
35. Suctioning			
36. Insertion of nasogastric tube			
37. Removal of nasogastric tube			
38. Upper GI series			
39. Lower GI series			
40. Enema			
41. Measuring blood pressure			
42. Removal of dressing			
43. Removal of electrodes			
44. Use of restraints			
45. Application of cast			
46. Removal of cast			
47. Traction			
48. Skeleton pins/wires			
Additional items:			

III. INFANT PAIN INVENTORY: Sources of Postoperative Pain

Pain Item	Pain Rating (0-10)	Quality Rating (0-10)	Comments
Postoperative site			
49. Thoracic	.....	.....	.....
50. Abdominal.....	.....	.....	.....
51. Skeletal.....	.....	.....	.....
52. Renal.....	.....	.....	.....
53. Genital/anal.....	.....	.....	.....
54. Cranial.....	.....	.....	.....
55. Otologic.....	.....	.....	.....
Procedures			
56. Change of dressing.....	.....	.....	.....
57. Wound care.....	.....	.....	.....
58. Removal of sutures	.....	.....	.....
59. Removal of staples.....	.....	.....	.....
60. Coughing.....	.....	.....	.....
61. Turning.....	.....	.....	.....
62. Deep breathing.....	.....	.....	.....
63. Ambulating	.....	.....	.....
Additional items:			
.....	.....	.....	.....
.....	.....	.....	.....
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IV. INFANT PAIN INVENTORY: Common Postnatal Health Conditions and Injuries

Pain Item	Pain Rating (0-10)	Quality Rating (0-10)	Comments
64. Colic			
65. Otitis media			
66. Gastroenteritis			
67. Urinary tract infection			
68. Diaper dermatitis			
69. Teething			
70. Falling			
71. Cuts			
72. Abrasions			
73. Fracture			
74. Electrical shock (minor)			
Burns			
75. First degree			
76. Second degree			
77. Third degree			

Additional items:

APPENDIX D

PERMISSIONS AND CORRESPONDENCE

OKLAHOMA STATE UNIVERSITY

CONSENT TO PARTICIPATE IN RESEARCH PROJECT

I, _____, agree to participate, and agree for my child, _____, to participate in the doctoral dissertation research project of Donna L. Wong, which has been approved by the Department of Family Relations and Child Development, OSU Institutional Review Board, and the child's pediatrician.

I understand that this research will be carried out by Donna Wong, assisted by Rosemary Liguori, both of whom are registered nurses and doctoral students, under the supervision of Dr. John C. McCullers. The purpose of this study is to learn if an infant's previous experience with pain has any effect on his/her reaction to the necessary but painful procedure of immunization and if there is any relationship between concurrent physiologic measurements and behavioral responses to pain.

I have been made aware of the research procedure, which will involve answering questions about my infant's development and pain experiences, taking of physiologic measures, such as pulse and blood pressure, which are part of the routine physical examination, and videotaping of my infant's reactions during the immunization. The interview and taping will take about 30 minutes. The information obtained by the researcher during this visit will be shared with my child's pediatrician.

I recognize that the major benefit that I will receive is the opportunity to discuss my infant's pain experiences with a professional nurse. I understand that there are no expected risks to my child or to myself.

By signing this consent form, I/I for my child acknowledge that our participation in this study is voluntary. I/I for my child also acknowledge that I have not waived any of my legal rights or released this institution from liability for negligence. I may revoke my consent and withdraw myself and my child from this study at any time. Records and results of this study will protect my family's confidentiality by not identifying me or my child by name. The videotapes will be viewed only by Ms. Wong, Dr. McCullers, and their immediate assistants under supervision for the purpose of data analysis. The viewing and storing of the tapes will be kept confidential and secure until the completion of the study, at which time they will be erased.

I have read this informed consent document. I/I for my child understand its contents and I/I for my child freely consent to participate in this study under the conditions described. I/I for my child will receive a copy of this signed consent form.

If I have questions about my/my child's rights as research subjects, I may consult with Donna Wong by calling 918-496-0544, Dr. John McCullers, College of Home Economics, Oklahoma State University, by calling 405-744-8360, or Terry Maciula, Office of University Research Services, 001 Life Sciences East, Oklahoma State University, by calling 405-744-9991.

_____ _____

Signature of Parent/participant Date

_____ _____

Signature of Principal Investigator Date

TULSA CITY-COUNTY HEALTH DEPARTMENT

4616 East 15th • 918 744-1000
Tulsa, Oklahoma 74112

February 9, 1990

Donna Lee Wong, R.N.,M.N.,P.N.P.
7535 South Urbana Avenue
Tulsa, Oklahoma 74136

Dear Ms. Wong:

I have reviewed your research proposal regarding pain in infants. I am pleased to grant permission for you to select subjects at the Child Health Clinic.

Sincerely,

Jerry G. Cleveland,P.E., D.Engr.
Interim Director

Geraldine Ling, R.N.,M.P.H.
Chief of Nursing

JC/GL:emt

CHILDREN'S CLINIC OF TULSA, INC.

– PROVIDING MEDICAL CARE FOR INFANTS, CHILDREN, & ADOLESCENTS –

–Office/Business Administrator–
Shellie C. Rogers

–Pediatricians–
B.J. Maguire, Jr., MD, FAAP
J.P. Hughes, MD, FAAP
Rick Cohen, MD
Perry Ward, MD

–Consultant–
R.K. Endres, MD, FAAP

May 8, 1989

Dr. Lloyd C. Faulkner
Chairman of the Institutional Review Board
Office of University Research Services
Oklahoma State University
001 Life Science East
Stillwater, Oklahoma 74078

Dear Dr. Faulkner:

I have met with Donna Wong and discussed fully her research project. I have agreed to participate to the extent that I will provide suitable subjects on which to conduct this research in my office here in Tulsa at the above address.

If you would like further information from me than is provided in this letter please feel free to contact me.

Sincerely,

J. Patrick Hughes MD

J. PATRICK HUGHES, M.D.

JPH/cs
cc: Donna L. Wong

DONNA LEE WONG, R.N., M.N., P.N.P.
Pediatric Nurse Author, Researcher, and Consultant

7535 South Urbana Avenue
Tulsa, Oklahoma 74136

Area Code - 918
496 - 0544

November 9, 1988

Dear :

Several months ago I discussed with you the possibility of your serving as a nurse expert regarding the development of an instrument to provide a quantitative measure of pain associated with various medical procedures or conditions that infants might experience. At this time I would like to formally request your participation in this project.

Presently, I am a doctoral candidate in family relations and child development at Oklahoma State University. My dissertation topic involves investigating the influence of previous painful experiences on the infant's responses to a painful stimulus. The instrument, the Infant Pain Inventory (IPI), will be used to provide a measure of an infant's previous pain experiences. The content validity for the IPI will be based on the opinions of nurse experts, like yourself, who have first-hand knowledge of infants' physiologic and behavioral responses to a wide variety of painful experiences.

Your responsibilities will include completing the enclosed Demographic Profile and 2 other forms (one that takes about 5 minutes to complete and one that will take about 20 minutes), which will be sent to you separately. Once the forms from all the nurse experts have been reviewed, I may ask a few additional questions. Your responses will be held in strictest confidence. The coded response forms will be seen only by my doctoral adviser, Dr. J. McCullers,and me, in connection with the data analysis. In publications, only group data will be reported.

Later phases of this research cannot be carried out until your responses have been received. Therefore, I would appreciate your completing the enclosed form and returning it to me at your earliest convenience and no later than **November 28, 1988** in the enclosed stamped self-addressed envelope.

Thank you so much for your initial indication of interest in this project. I hope you will be able to participate. Your expertise is critical to the successful conduct of this research.

Sincerely yours,

Donna L. Wong, RN, MN, PNP
Doctoral Candidate

Enc.

APPENDIX E

SELECTED STATISTICAL ANALYSIS

ADDITIONAL SUMMARY TABLES

TABLE I

MAXIMUM FRACTIONAL INCREASE IN HEART RATE -- BY AGE (MONTHS) AND SEX

Age		2	4	6	15	18
Male	M	0.2447	0.2669	0.2867	0.2364	0.2168
	SD	0.6664	0.1462	0.1971	0.1500	0.1336
Female	M	0.3091	0.2286	0.2776	0.2699	0.4424
	SD	0.1715	0.1291	0.1083	0.1002	0.2356

TABLE II

MAXIMUM FRACTIONAL INCREASE IN HEART RATE -- BY AGE (MONTHS) AND RACE

Age		2	4	6	15	18
White	M	0.2614	0.2260	0.1951	0.2261	0.3198
	SD	0.1226	0.9868	0.1048	0.1179	0.1666
Non-white	M	0.2968	0.2776	0.3704	0.3560	0.3379
	SD	0.1461	0.1843	0.1923	0.8074	0.4390

TABLE III

TIME (SECONDS) TO MAXIMUM FRACTIONAL INCREASE IN HEART RATE -- BY AGE (MONTHS) AND SEX

Age		2	4	6	15	18
Male	M	64.91	48.74	36.56	42.02	22.06
	SD	39.05	20.56	19.38	12.14	78.84
Female	M	63.39	48.98	41.28	45.74	57.98
	SD	21.52	15.01	17.62	15.30	31.93

TABLE IV

TIME (SECONDS) TO MAXIMUM FRACTIONAL INCREASE IN HEART RATE -- BY AGE (MONTHS) AND RACE

Age		2	4	6	15	18
White	M	70.40	53.20	38.46	46.91	45.27
	SD	35.68	16.35	17.31	13.88	31.92
Non-white	M	56.12	41.69	44.08	34.00	26.50
	SD	22.12	16.94	21.33	7.23	(n = 1)

TABLE V

TIME (SECONDS) TO INITIAL CRY -- BY AGE (MONTHS) AND SEX

Age		2	4	6	15	18
Male	M	1.44	1.96	1.99	1.74	1.27
	SD	0.36	0.90	0.92	0.11	0.93
Female	M	1.99	3.44	2.34	2.57	1.56
	SD	1.37	1.01	1.18	0.66	0.90

TABLE VI

TIME (SECONDS) TO INITIAL CRY -- BY AGE (MONTHS) AND RACE

Age		2	4	6	15	18
White	M	1.57	2.72	2.30	2.30	1.44
	SD	0.49	1.31	1.19	0.92	0.86
Non-white	M	1.77	2.81	2.04	2.56	1.25
	SD	1.20	1.06	0.70	0.53	1.34

TABLE VII

TIME (SECONDS) TO SOOTHING --
BY AGE (MONTHS) AND SEX

Age		2	4	6	15	18
Male	M	95.19	54.93	102.18	84.51	69.67
	SD	27.97	18.16	46.39	32.01	38.90
Female	M	88.80	60.95	90.01	79.68	53.73
	SD	80.61	29.89	35.07	46.93	19.15

TABLE VIII

TIME (SECONDS) TO SOOTHING --
AGE (MONTHS) VS RACE

Age		2	4	6	15	18
White	M	79.20	65.15	85.58	90.28	63.63
	SD	16.98	21.93	34.43	45.91	34.56
Non-white	M	102.23	35.12	130.14	56.58	58.10
	SD	24.75	35.88	37.40	23.49	10.56

TABLE IX

MAXIMUM FRACTIONAL INCREASE IN HEART RATE AMONG SUBJECTS WHO SOOTHED OR DID NOT SOOTHE WITH LOW VS HIGH PAIN HISTORY

	Low pain history		High pain history		t Test[a]
Age (mos.)	N	Mean maximum increase	N	Mean maximum increase	
			Soothed group		
2	7	0.2345	-	-	-
4	5	0.1656	2	0.2782	1.031 (df, 5)
6	11	0.2469	10	0.2096	0.540 (df, 19)
15	6	0.2601	5	0.2645	0.050 (df, 9)
18	-	-	-	-	-
			Not Soothed group		
2	6	0.3028	2	0.3160	0.077 (df, 6)
4	3	0.3448	3	0.2800	0.358 (df, 4)
6	2	0.3342	3	0.2476	0.474 (df, 3)
15	-	-	3	0.2647	-
18	-	-	-	-	-

[a]Not significant at $p<.05$.

c:ph-rmax.tab

TABLE IX

TIME TO INITIAL CRY AMONG SUBJECTS WHO SOOTHED OR DID NOT SOOTHE

Soothed				Not soothed				t Test[a]
Mean age (mos.)	N	Mean time (seconds)	(SD)[b]	Mean age (mos.)	N	Mean time (seconds)	(SD)[b]	
2.12	8	1.40	(0.47)	2.2	5	2.16	(1.40)	1.289 (df,11)
4.30	10	3.11	(1.13)	4.4	5	2.03	(1.08)	1.660 (df,13)
6.78	18	2.43	(1.14)	6.5	4	1.45	(0.33)	1.609 (df,20)
15.70	10	2.47	(0.79)	16.0	1	1.3	-	- [c]
18.60	10	1.30	(0.86)	20.0	1	2.45	-	- [c]

[a]Not significant at $p<.05$.

[b]Standard deviation.

[c]Not calculated due to small ns in unsoothed groups.

TABLE X

MAXIMUM FRACTIONAL INCREASE IN HEART RATE AMONG SUBJECTS WHO SOOTHED OR DID NOT SOOTHE WITH LOW VS HIGH PAIN HISTORY

	Low pain history		High pain history		t Test[a]
Age (mos.)	N	Mean maximum increase	N	Mean maximum increase	
			Soothed group		
2	7	0.2345	-	-	-
4	5	0.1656	2	0.2782	1.031 (df, 5)
6	11	0.2469	10	0.2096	0.540 (df, 19)
15	6	0.2601	5	0.2645	0.050 (df, 9)
18	-	-	-	-	-
			Not Soothed group		
2	6	0.3028	2	0.3160	0.077 (df, 6)
4	3	0.3448	3	0.2800	0.358 (df, 4)
6	2	0.3342	3	0.2476	0.474 (df, 3)
15	-	-	3	0.2647	-
18	-	-	-	-	-

[a]Not significant at $p<.05$.

TABLE XI

TIME TO MAXIMUM FRACTIONAL INCREASE IN HEART RATE AMONG SUBJECTS WHO SOOTHED OR DID NOT SOOTHE WITH LOW VS HIGH PAIN HISTORY

	Low pain history		High pain history		t Test[a]
Age (mos.)	N	Mean time (seconds)	N	Mean time (seconds)	
			Soothed group		
2	7	52.94	-	-	-
4	5	51.03	2	56.15	0.330 (df, 5)
6	11	40.06	10	34.81	0.716 (df, 9)
15	6	48.27	5	39.69	0.961 (df, 9)
18	-	-	4	45.38	-
			Not Soothed group		
2	6	64.59	2	97.86	0.869 (df, 6)
4	3	53.80	3	55.09	0.067 (df, 4)
6	-	-	3	67.02	-
15	-	-	3	43.34	-
18	-	-	-	-	-

[a]Not significant at $p<.05$.

TABLE XII

TIME TO INITIAL CRY AMONG SUBJECTS WHO SOOTHED OR DID NOT SOOTHE WITH LOW VS HIGH PAIN HISTORY

	Low pain history		High pain history		t Test[a]
Age (mos.)	N	Mean time (seconds)	N	Mean time (seconds)	
			Soothed group		
2	7	1.30	-	-	-
4	6	3.25	2	3.41	0.130 (df, 6)
6	9	2.19	9	2.66	0.818 (df, 16)
15	7	2.34	3	2.76	0.701 (df, 8)
18	4	1.72	6	1.02	1.185 (df, 8)
			Not Soothed group		
2	3	2.32	2	1.92	0.223 (df,3)
4	2	2.12	2	1.44	0.339 (df, 2)
6	3	1.59	-	-	-
15	-	-	-	-	-
18	-	-	-	-	-

[a]Not significant at $p<.05$.

TABLE XIII

SOOTHING TIME FOR SUBJECTS WITH LOW VS HIGH PAIN HISTORY

	Low pain history		High pain history		t Test[a]
Age (mos.)	N	Mean time (seconds)	N	Mean time (seconds)	
2	7	95.07	-	-	-
4	6	66.10	2	52.36	0.511 (df, 6)
6	11	88.19	10	10.36	0.881 (df, 19)
15	7	93.42	4	56.10	1.199 (df, 9)
18	2	30.90	5	69.18	0.985 (df, 5)

[a]Not significant at $p<.05$.

ANALYSES OF VARIANCE

(RMAX-RO)/RO VS SEX AND AGE

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
ROWS	.375228E-01	1	.375228E-01	1.76
COLUMNS	.864167E-01	4	.216042E-01	1.01
AXB	.244451E+00	4	.611126E-01	2.87
SS/AB	.178835E+01	84	.212899E-01	

(RMAX-RO)/RO VS RACE AND AGE

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
ROWS	.115211E+00	1	.115211E+00	5.21
COLUMNS	.421972E-01	4	.105493E-01	.48
AXB	.622282E-01	4	.155571E-01	.70
SS/AB	.185684E+01	84	.221053E-01	

(RMAX-RO)/RO FOR SOOTHED AND NOT SOOTHED VS AGE

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
ROWS	.845919E-01	1	.845919E-01	3.64
COLUMNS	.957994E-01	4	.239499E-01	1.03
AXB	.264258E-01	4	.660646E-02	.28
SS/AB	.194957E+01	84	.232091E-01	

(RMAX-RO)/RO FOR SOOTHED AND NOT SOOTHED, AGE 2-21

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
MEAN	.652026E+01	1	.652026E+01	
TREATMENTS	.102797E+00	1	.102797E+00	4.59
ERROR	.205858E+01	92	.223759E-01	
TOTALS	.868164E+01	93		

TIME TO MAXIMUM PULSE RATE VS SEX AND AGE

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
ROWS	.120094E+04	1	.120094E+04	2.62
COLUMNS	.545102E+04	4	.136275E+04	2.97
AXB	.309742E+04	4	.774355E+03	1.69
SS/AB	.321014E+05	70	.458592E+03	

TIME TO REACH MAXIMUM HEART RATE FOR WHITES AND NONWHITES VS AGE

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
ROWS	.115670E+04	1	.115670E+04	2.50
COLUMNS	.391080E+04	4	.977701E+03	2.11
AXB	.751789E+03	4	.187947E+03	.41
SS/AB	.323589E+05	70	.462270E+03	

TIME TO REACH MAXIMUM HEART RATE FOR SOOTHED AND NOT SOOTHED

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
MEAN	.180185E+06	1	.180185E+06	
TREATMENTS	.332945E+04	1	.332945E+04	6.91
ERROR	.376084E+05	78	.482159E+03	
TOTALS	.221123E+06	79		

TIME TO REACH MAXIMUM HEART RATE FOR SOOTHED AND NOT SOOTHED & AGE

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
ROWS	.106481E+04	1	.106481E+04	2.35
COLUMNS	.303506E+04	4	.758766E+03	1.67
AXB	.968063E+03	4	.242016E+03	.53

TIME TO MINIMUM OXYGEN SATURATION (BELOW 95%) FOR AGE 2-21

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
MEAN	.118226E+06	1	.118226E+06	
TREATMENTS	.778687E+04	4	.194672E+04	1.71
ERROR	.672768E+05	59	.114028E+04	
TOTALS	.193290E+06	63		

TIME TO MINIMUM OXYGEN SATURATION (AT OR BELW 100.0%) FOR AGE 2-21

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
MEAN	.167390E+06	1	.167390E+06	
TREATMENTS	.905870E+04	4	.226468E+04	2.19
ERROR	.878615E+05	85	.103366E+04	
TOTALS	.264310E+06	89		

INITIAL CRYING TIME FOR SOOTHED AND NOT SOOTHED

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
MEAN	.329432E+03	1	.329432E+03	
TREATMENTS	.121252E+01	1	.121252E+01	.99
ERROR	.855174E+02	70	.122168E+01	
TOTALS	.416162E+03	71		

INITIAL CRYING TIME VS SEX AND AGE

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
ROWS	.751309E+01	1	.751309E+01	7.70
COLUMNS	.117845E+02	4	.294613E+01	3.02
AXB	.281967E+01	4	.704918E+00	.72
SS/AB	.605125E+02	62	.976008E+00	

INITIAL CRYING TIME

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
MEAN	.329432E+03	1	.329432E+03	
TREATMENTS	.148618E+02	4	.371546E+01	3.46
ERROR	.718681E+02	67	.107266E+01	

SOOTHING TIME VS SEX AND AGE

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
ROWS	.500469E+03	1	.500469E+03	.38
COLUMNS	.135599E+05	4	.338998E+04	2.59
AXB	.955906E+03	4	.238977E+03	.18
SS/AB	.772794E+05	59	.130982E+04	

SOOTHING TIME VS RACE AND AGE

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
ROWS	.250000E+00	1	.250000E+00	.00
COLUMNS	.184875E+05	4	.462186E+04	4.06
AXB	.935313E+04	4	.233828E+04	2.06
SS/AB	.671169E+05	59	.113757E+04	

SOOTHING TIME FOR AGE GROUP 2-21

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
MEAN	.431821E+06	1	.431821E+06	
TREATMENTS	.151669E+05	4	.379173E+04	3.06
ERROR	.791771E+05	64	.123714E+04	
TOTALS	.526165E+06	68		

ABSOLUTE DIFFERENCE BETWEEN TMAX AND TMIN VS AGE

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
MEAN	.589830E+05	1	.589830E+05	
TREATMENTS	.169795E+05	4	.424487E+04	7.91
ERROR	.381164E+05	71	.536851E+03	
TOTALS	.114079E+06	75		

(RMAX-RO)/RO FOR HIGH AND LOW PAIN HISTORY

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
MEAN	.641536E+01	1	.641536E+01	
TREATMENTS	.535011E-03	1	.535011E-03	.02
ERROR	.207902E+01	86	.241747E-01	
TOTALS	.849492E+01	87		

TIME TO MAXIMUM PULSE RATE FOR HIGH AND LOW PAIN HISTORY

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
MEAN	.179240E+06	1	.179240E+06	
TREATMENTS	.585938E+02	1	.585938E+02	.11
ERROR	.382448E+05	74	.516822E+03	
TOTALS	.217543E+06	75		

1NITIAL CRYING TIME FOR HIGH AND LOW PAIN HISTORY

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
MEAN	.312184E+03	1	.312184E+03	
TREATMENTS	.430298E-02	1	.430298E-02	.00
ERROR	.815235E+02	66	.123520E+01	
TOTALS	.393711E+03	67		

SOOTHING TIME FOR HIGH AND LOW PAIN HISTORY

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
MEAN	.422032E+06	1	.422032E+06	
TREATMENTS	.333563E+03	1	.333563E+03	.23
ERROR	.892351E+05	62	.143928E+04	
TOTALS	.511601E+06	63		

(RM-RO)/RO VS HIGH AND LOW PAIN HISTORY, AND SOOTHED & NOT SOOTHED

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
ROWS	.163088E-01	1	.163088E-01	.71
COLUMNS	.131510E+00	1	.131510E+00	5.76
AXB	.309520E-01	1	.309520E-01	1.36
SS/AB	.191726E+01	84	.228245E-01	

TRMAX VS HIGH AND LOW PAIN HISTORY, AND SOOTHED NOT SOOTHED

SOURCE OF VARIATION	SUM OF SQUARES	D. F.	MEAN SQUARE	F VALUE
ROWS	.208703E+03	1	.208703E+03	.44
COLUMNS	.366125E+04	1	.366125E+04	7.81
AXB	.992703E+03	1	.992703E+03	2.12
SS/AB	.337682E+05	72	.469003E+03	

REGRESSION ANALYSES

MAXIMUM FRACTIONAL INCREASE IN PULSE RATE VS AGE

VARIABLE 0 = INTERCEPT
VARIABLE 1 = AGE
VARIABLE 2 = AGE*AGE
VARIABLE 3 (DEPENDENT VARIABLE) = MFIIPR
EQUATION FITTED IS Y = AO + A1*X + A2*X**2

NO. OF INDEPENDENT VARIABLES 2 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.94940400E+01	.72296080E+01	.5645
2	.13195060E+03	.15413720E+03	.6822
3	.26654400E+00	.35668880E-01	1.0000

CORRELATION BETWEEN INDEPENDENT VARIABLES

1 2 .9878

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.48649010E-02	2	.24324510E-02	21.70
RESIDUAL	.22414330E-03	2	.11207160E-03	
TOTAL	.50890450E-02	4	.12722610E-02	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.32061050E+00	.29462710E-03
1	-.22153100E-01	.22018760E-04
2	.11841940E-02	.48440370E-07

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .95596

INDEPENDENT VARIABLE	DEPENDENT VARIABLE		DIFFERENCE	PCT. ERR.
	OBSERVED	CALCULATED		
2.18750	.27689	.27782	.00093	.3337161E+00
4.25000	.24319	.24785	.00466	.1879890E+01
6.77780	.23408	.22486	-.00922	-.4099696E+01
15.66670	.25501	.26420	.00919	.3478249E+01
18.58820	.32355	.31799	-.00556	-.1749039E+01

TIME ELAPSED FOR PULSE TO REACH MAXIMUM AFTER NEEDLE IN VS AGE

VARIABLE 0 = INTERCEPT
VARIABLE 1 = AGE
VARIABLE 2 (DEPENDENT VARIABLE) + TRMAX
EQUATION FITTED IS Y = A0 + A1*X

NO. OF INDEPENDENT VARIABLES 1 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.94716400E+01	.71968170E+01	-.6273
2	.47988740E+02	.96911000E+01	1.0000

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.14783890E+03	1	.14783890E+03	1.95
RESIDUAL	.22783200E+03	3	.75944010E+02	
TOTAL	.37567090E+03	4	.93917720E+02	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.55989840E+02	.48074200E+02
1	-.84474300E+00	.36656640E+00

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .39353

INDEPENDENT VARIABLE	DEPENDENT VARIABLE		DIFFERENCE	PCT. ERR.
	OBSERVED	CALCULATED		
2.18750	64.15312	54.14197	-10.01115	-.1849056E+02
4.25000	49.34999	52.39968	3.04969	.5820062E+01
6.77780	39.70630	50.26434	10.55804	.2100504E+02
15.64290	44.14572	42.77561	-1.37011	-.3203016E+01
18.50000	42.58857	40.36210	-2.22647	-.5516242E+01

TIME ELAPSED FOR PULSE TO REACH MAXIMUM AFTER NEEDLE IN VS AGE

VARIABLE 0 = INTERCEPT
VARIABLE 1 = AGE
VARIABLE 2 = AGE*AGE
VARIABLE 3 (DEPENDENT VARIABLE) = TRMAX
EQUATION FITTED IS Y = A0 + A1*X + A2*X**2

NO. OF INDEPENDENT VARIABLES 2 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.94716400E+01	.71968170E+01	-.6273
2	.13114730E+03	.15286820E+03	-.5176
3	.47988740E+02	.96911000E+01	1.0000

CORRELATION BETWEEN INDEPENDENT VARIABLES

1 2 .9878

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.30993260E+03	2	.15496630E+03	4.71
RESIDUAL	.65738280E+02	2	.32869140E+02	
TOTAL	.37567090E+03	4	.93917720E+02	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.74089890E+02	.87267910E+02
1	-.64633940E+01	.65630330E+01
2	.26777600E+00	.14546260E-01

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .82501

INDEPENDENT VARIABLE	DEPENDENT VARIABLE		DIFFERENCE	PCT. ERR.
	OBSERVED	CALCULATED		
2.18750	64.15312	61.23257	-2.92056	-.4769611E+01
4.25000	49.34999	51.45717	2.10718	.4095020E+01
6.77780	39.70630	42.58355	2.87725	.6756711E+01
15.64290	44.14572	38.50854	-5.63718	-.1463879E+02
18.50000	42.58857	46.16344	3.57487	.7743937E+01

TIME TO MINIMUM OXYGEN SATURATION (LESS THAN 95%) VS AGE

VARIABLE 0 = INTERCEPT
VARIABLE 1 = AGE
VARIABLE 2 = AGE*AGE
VARIABLE 3 (DEPENDENT VARIABLE) = TMIN
EQUATION FITTED IS Y = A0 + A1*X + A2*X**2

NO. OF INDEPENDENT VARIABLES 2 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.94964010E+01	.71996800E+01	-.6425
2	.13164990E+03	.15353760E+03	-.5217
3	.42809070E+02	.12197990E+02	1.0000

CORRELATION BETWEEN INDEPENDENT VARIABLES

1 2 .9880

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.56547660E+03	2	.28273830E+03	19.05
RESIDUAL	.29687500E+02	2	.14843750E+02	
TOTAL	.59516410E+03	4	.14879100E+03	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.78984770E+02	.40415650E+02
1	-.90429620E+01	.30086990E+01
2	.37751610E+00	.66156900E-02

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .95012

INDEPENDENT VARIABLE	DEPENDENT VARIABLE		DIFFERENCE	PCT. ERR.
	OBSERVED	CALCULATED		
2.21430	58.85000	60.81195	1.96195	.3226255E+01
4.33330	51.26250	46.88771	-4.37479	-.9330356E+01
6.72220	32.66722	35.25536	2.58814	.7341121E+01
15.66670	30.13111	29.97103	-.16008	-.5341284E+00
18.54550	41.13454	41.11974	-.01480	-.3598566E-01

INITIAL CRYING TIME VS AGE

VARIABLE 0 = INTERCEPT
VARIABLE 1 = AGE
VARIABLE 2 (DEPENDENT VARIABLE) = TIC

NO. OF INDEPENDENT VARIABLES 1 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.95338000E+01	.72846750E+01	-.3661
2	.20886080E+01	.53728000E+00	1.0000

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.15476420E+00	1	.15476420E+00	.46
RESIDUAL	.99991230E+00	3	.33330410E+00	
TOTAL	.11546760E+01	4	.28866910E+00	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.23460420E+01	.20938330E+00
1	-.27002270E-01	.15702190E-02

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .13403

INDEPENDENT VARIABLE	DEPENDENT VARIABLE		DIFFERENCE	PCT. ERR.
	OBSERVED	CALCULATED		
2.15380	1.69692	2.28788	.59096	.2583018E+02
4.33330	2.75067	2.22903	-.52164	-.2340193E+02
6.72730	2.24909	2.16439	-.08470	-.3913348E+01
15.72730	2.34454	1.92137	-.42317	-.2202444E+02
18.72730	1.40182	1.84036	.43854	.2382914E+02

INITIAL CRYING TIME VS AGE

VARIABLE 0 = INTERCEPT
VARIABLE 1 = AGE
VARIABLE 2 = AGE*AGE
VARIABLE 3 (DEPENDENT VARIABLE) = TIC
EQUATION FITTED IS Y = A0 + A1*X + A2*X**2

NO. OF INDEPENDENT VARIABLES 2 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.95338000E+01	.72846750E+01	-.3661
2	.13334650E+03	.15628140E+03	-.4754
3	.20886080E+01	.53728000E+00	1.0000

CORRELATION BETWEEN INDEPENDENT VARIABLES

1 2 .9876

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.76156620E+00	2	.38078310E+00	1.94
RESIDUAL	.39311030E+00	2	.19655510E+00	
TOTAL	.11546760E+01	4	.28866910E+00	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.12566690E+01	.50781440E+00
1	.30921620E+00	.37536490E-01
2	-.15869000E-01	.81556650E-04

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .65955

INDEPENDENT VARIABLE	DEPENDENT VARIABLE		DIFFERENCE	PCT. ERR.
	OBSERVED	CALCULATED		
2.15380	1.69692	1.84904	.15212	.8227190E+01
4.33330	2.75067	2.29861	-.45205	-.1966641E+02
6.72730	2.24909	2.61868	.36959	.1411367E+02
15.72730	2.34454	2.19464	-.14990	-.6830356E+01
18.72730	1.40182	1.48201	.08019	.5410678E+01

SOOTHING TIME VS AGE

VARIABLE 0 = INTERCEPT
VARIABLE 1 = AGE
VARIABLE 2 (DEPENDENT VARIABLE) = TS
EQUATION FITTED IS Y = A0 + A1*X

NO. OF INDEPENDENT VARIABLES 1 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.94802400E+01	.72427410E+01	-.4547
2	.76996960E+02	.17682840E+02	1.0000

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.25859380E+03	1	.25859380E+03	.78
RESIDUAL	.99213870E+03	3	.33071290E+03	
TOTAL	.12507320E+04	4	.31268310E+03	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.87521280E+02	.20779500E+03
1	-.11101320E+01	.15761050E+01

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .20675

INDEPENDENT VARIABLE	DEPENDENT VARIABLE		DIFFERENCE	PCT. ERR.
	OBSERVED	CALCULATED		
2.12500	93.59000	85.16225	-8.42775	-.9896110E+01
4.30000	59.14600	82.74771	23.60171	.2852250E+02
6.76190	94.23714	80.01468	-14.22246	-.1777481E+02
15.50000	79.77167	70.31423	-9.45744	-.1345024E+02
18.71430	58.24000	66.74594	8.50594	.1274376E+02

SOOTHING TIME VS AGE(SINGLE SHOT)

VARIABLE 0 = INTERCEPT
VARIABLE 1 = AGE
VARIABLE 2 = AGE*AGE
VARIABLE 3 (DEPENDENT VARIABLE) = TS
EQUATION FITTED IS Y = A0 + A1*X + A2*X**2

NO. OF INDEPENDENT VARIABLES 2 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.94802400E+01	.72427410E+01	-.4547
2	.13184080E+03	.15485520E+03	-.4902
3	.76996960E+02	.17682840E+02	1.0000

CORRELATION BETWEEN INDEPENDENT VARIABLES

1 2 .9868

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.34067970E+03	2	.17033980E+03	.37
RESIDUAL	.91005270E+03	2	.45502640E+03	
TOTAL	.12507320E+04	4	.31268310E+03	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.75220060E+02	.11247560E+04
1	.26968210E+01	.82511210E+02
2	-.18044180E+00	.18049590E+00

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .27238

INDEPENDENT VARIABLE	DEPENDENT VARIABLE		DIFFERENCE	PCT. ERR.
	OBSERVED	CALCULATED		
2.12500	93.59000	80.13600	-13.45399	-.1678895E+02
4.30000	59.14600	83.48002	24.33402	.2914951E+02
6.76190	94.23714	85.20531	-9.03183	-.1060008E+02
15.50000	79.77167	73.66965	-6.10201	-.8282939E+01
18.71430	58.24000	62.49395	4.25395	.6806982E+01

PROPORTION OF CHILDREN WITH TOTAL PHYSICAL DISTRESS
FACE BEFORE BANDAID VS AGE (SINGLE SHOT)

VARIABLE 0 = INTERCEPT OR THE CONSTANT A0
VARIABLE 1 = AGE
VARIABLE 2 (DEPENDENT VARIABLE) = PROPORTION
EQUATION FITTED IS P = A0*(AGE)**A1

NO. OF INDEPENDENT VARIABLES 1 NO. OF OBSERVATIONS 4

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.22630120E+01	.69940500E+00	-.9980
2	-.18668850E+00	.15447360E+00	1.0000

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.71304920E-01	1	.71304920E-01	506.80
RESIDUAL	.28139350E-03	2	.14069680E-03	
TOTAL	.71586310E-01	3	.23862100E-01	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.31214660E+00	.52617170E-03
1	-.22042980E+00	.95875020E-04

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .99607

EXP(INTERCEPT)= .13663550E+01

OBSERVED	COMPUTED	DIFFERENCE	PCT
1.00000	.99169	-.00831	-.8382807E+00
.88460	.89635	.01175	.1310752E+01
.75000	.74549	-.00451	-.6052186E+00
.71430	.71515	.00085	.1186428E+00

PROPORTION OF CHILDREN WITH TOTAL PHYSICAL DISTRESS
FACE AFTER BANDAID VS AGE (SINGLE SHOT)

VARIABLE 0 = INTERCEPT OR THE CONSTANT A0
VARIABLE 1 = AGE
VARIABLE 2 (DEPENDENT VARIABLE) = PROPORTION
EQUATION FITTED IS P = A0*(AGE)**A1

NO. OF INDEPENDENT VARIABLES 1 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.19718400E+01	.90434090E+00	-.9857
2	-.22708640E+01	.13975870E+01	1.0000

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.75915950E+01	1	.75915950E+01	102.86
RESIDUAL	.22141270E+00	3	.73804220E-01	
TOTAL	.78130070E+01	4	.19532520E+01	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.73296730E+00	.10248110E+00
1	-.15233650E+01	.22560900E-01

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .97166

EXP(INTERCEPT)= .20812470E+01

OBSERVED	COMPUTED	DIFFERENCE	PCT
.62500	.63053	.00553	.8764121E+00
.18750	.22965	.04215	.1835242E+02
.16000	.11223	-.04777	-.4256446E+02
.02500	.03116	.00616	.1976735E+02
.02500	.02314	-.00186	-.8023432E+01

PROPORTION OF TOTAL + PREDOMINANTLY PHYSICALLY DISTRESSED
FACE AFTER BANDAID VS AGE (SINGLE SHOT)

VARIABLE 0 = INTERCEPT
VARIABLE 1 = AGE
VARIABLE 2 = AGE*AGE
VARIABLE 3 (DEPENDENT VARIABLE) = PROPORTION
EQUATION FITTED IS Y = A0 + A1*X + A2*X**2

NO. OF INDEPENDENT VARIABLES 2 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.96360000E+01	.74333360E+01	-.8234
2	.13705610E+03	.16237440E+03	-.7252
3	.46942000E+00	.27174440E+00	1.0000

CORRELATION BETWEEN INDEPENDENT VARIABLES

1 2 .9870

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.28745200E+00	2	.14372600E+00	36.26
RESIDUAL	.79284910E-02	2	.39642450E-02	
TOTAL	.29538050E+00	4	.73845120E-01	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.11588450E+01	.97089910E-02
1	-.15190650E+00	.69237620E-03
2	.56498490E-02	.14510240E-05

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .97316

INDEPENDENT VARIABLE	DEPENDENT VARIABLE		DIFFERENCE	PCT. ERR.
	OBSERVED	CALCULATED		
2.19000	.81250	.85327	.04077	.4777762E+01
4.25000	.68750	.61529	-.07221	-.1173539E+02
6.80000	.36000	.38713	.02713	.7007990E+01
15.77000	.15380	.16836	.01456	.8646663E+01
19.17000	.33330	.32305	-.01025	-.3171409E+01

MEAN TPS-TS IN SECONDS VS AGE IN MONTHS

VARIABLE 0 = INTERCEPT
VARIABLE 1 = AGE
VARIABLE 2 (DEPENDENT VARIABLE) = TPS-TS
EQUATION FITTED IS Y = A0 + A1*X

NO. OF INDEPENDENT VARIABLES 1 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.93960720E+01	.72642550E+01	-.4281
2	.31927250E+02	.12342500E+02	1.0000

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.11169780E+03	1	.11169780E+03	.67
RESIDUAL	.49765090E+03	3	.16588360E+03	
TOTAL	.60934860E+03	4	.15233720E+03	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.38762420E+02	.10255990E+03
1	-.72744980E+00	.78588940E+00

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .18331

INDEPENDENT VARIABLE	DEPENDENT VARIABLE		DIFFERENCE	PCT. ERR.
	OBSERVED	CALCULATED		
2.00000	23.91875	37.30752	13.38877	.3588758E+02
4.14286	52.94286	35.74870	-17.19416	-.4809732E+02
6.68750	32.68563	33.89759	1.21196	.3575368E+01
15.75000	23.01501	27.30508	4.29007	.1571162E+02
18.40000	27.07400	25.37734	-1.69666	-.6685725E+01

MEAN TPS-TS IN SECONDS VS AGE IN MONTHS

VARIABLE 0 = INTERCEPT
VARIABLE 1 = AGE
VARIABLE 2 = AGE*AGE
VARIABLE 3 (DEPENDENT VARIABLE) = TPS-TS
EQUATION FITTED IS Y = A0 + A1*X + A2*X**2

NO. OF INDEPENDENT VARIABLES 2 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.93960720E+01	.72642550E+01	-.4281
2	.13050170E+03	.15273760E+03	-.4630
3	.31927250E+02	.12342500E+02	1.0000

CORRELATION BETWEEN INDEPENDENT VARIABLES

1 2 .9877

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.15190820E+03	2	.75954100E+02	.33
RESIDUAL	.45744040E+03	2	.22872020E+03	
TOTAL	.60934860E+03	4	.15233720E+03	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.30170730E+02	.56138200E+03
1	.20331310E+01	.44440840E+02
2	-.13292450E+00	.10052460E+00

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .24930

INDEPENDENT VARIABLE	DEPENDENT VARIABLE		DIFFERENCE	PCT. ERR.
	OBSERVED	CALCULATED		
2.00000	23.91875	33.70530	9.78655	.2903564E+02
4.14286	52.94286	36.31229	-16.63057	-.4579874E+02
6.68750	32.68563	37.82256	5.13693	.1358165E+02
15.75000	23.01501	29.21896	6.20395	.2123262E+02
18.40000	27.07400	22.57743	-4.49657	-.1991623E+02

/TRMAX-TMIN/ VS AGE

VARIABLE 0 = INTERCEPT
VARIABLE 1 = AGE
VARIABLE 2 = AGE*AGE
VARIABLE 3 (DEPENDENT VARIABLE) = /TRMAX-TMIN/
EQUATION FITTED IS Y = A0 + A1*X + A2*X**2

NO. OF INDEPENDENT VARIABLES 2 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.95404610E+01	.72914710E+01	-.5213
2	.13355280E+03	.15711110E+03	-.3779
3	.28834070E+02	.16108750E+02	1.0000

CORRELATION BETWEEN INDEPENDENT VARIABLES

1 2 .9870

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.10299680E+04	2	.51498410E+03	128.78
RESIDUAL	.79980470E+01	2	.39990230E+01	
TOTAL	.10379660E+04	4	.25949160E+03	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.77301720E+02	.10022690E+02
1	-.12647170E+02	.72540650E+00
2	.54055110E+00	.15624200E-02

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .99229

INDEPENDENT VARIABLE	DEPENDENT VARIABLE		DIFFERENCE	PCT. ERR.
	OBSERVED	CALCULATED		
2.18750	53.62812	52.22266	-1.40546	-.2691284E+01
4.26670	31.12800	33.18064	2.05264	.6186261E+01
6.80770	16.49231	16.25532	-.23699	-.1457923E+01
15.58330	12.60333	11.48415	-1.11918	-.9745474E+01
18.85710	30.31857	31.02752	.70896	.2284925E+01

PAIN HISTORY VS AGE

VARIABLE 0 = INTERCEPT
VARIABLE 1 = AGE
VARIABLE 2 (DEPENDENT VARIABLE) = PAIN HISTORY
EQUATION FITTED IS Y = A0 + A1*X

NO. OF INDEPENDENT VARIABLES 1 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.94504600E+01	.72558960E+01	.9037
2	.69550760E+01	.12339900E+01	1.0000

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.49739230E+01	1	.49739230E+01	13.36
RESIDUAL	.11170200E+01	3	.37233990E+00	
TOTAL	.60909420E+01	4	.15227360E+01	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.55026850E+01	.23237570E+00
1	.15368450E+00	.17680620E-02

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .81661

INDEPENDENT VARIABLE	DEPENDENT VARIABLE		DIFFERENCE	PCT. ERR.
	OBSERVED	CALCULATED		
2.17650	5.52941	5.83718	.30777	.5272577E+01
4.08330	5.91667	6.13023	.21356	.3483646E+01
6.77270	7.09091	6.54354	-.54737	-.8364972E+01
15.63160	8.47368	7.90502	-.56866	-.7193648E+01
18.58820	7.76471	8.35940	.59469	.7114068E+01

PROPORTION SOOTHED VS MEAN AGE (LOW PAIN HISTORY)

VARIABLE 0 = INTERCEPT
VARIABLE 1 = AGE
VARIABLE 2 = AGE*AGE
VARIABLE 3 (DEPENDENT VARIABLE) = PROPORTION SOOTHED
EQUATION FITTED IS Y = A0 + A1*X + A2*X**2

NO. OF INDEPENDENT VARIABLES 2 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.93925600E+01	.71545880E+01	.5692
2	.12917070E+03	.15154300E+03	.4447
3	.75314000E+00	.17652960E+00	1.0000

CORRELATION BETWEEN INDEPENDENT VARIABLES

1 2 .9886

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.11706160E+00	2	.58530810E-01	15.42
RESIDUAL	.75895790E-02	2	.37947890E-02	
TOTAL	.12465120E+00	4	.31162800E-01	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	.21131560E+00	.10710620E-01
1	.14118990E+00	.81866590E-03
2	-.60718750E-02	.18247520E-05

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .93911

INDEPENDENT VARIABLE	DEPENDENT VARIABLE		DIFFERENCE	PCT. ERR.
	OBSERVED	CALCULATED		
2.30770	.53850	.50480	-.03370	-.6675090E+01
4.11110	.66670	.68914	.02244	.3256184E+01
6.61540	.84620	.87962	.03342	.3798980E+01
15.50000	1.00000	.94099	-.05901	-.6270998E+01
18.42860	.71430	.75116	.03686	.4906796E+01

PROPORTION SOOTHED VS MEAN AGE (HIGH PAIN HISTORY)

VARIABLE 0 = INTERCEPT
VARIABLE 1 = AGE
VARIABLE 2 = AGE*AGE
VARIABLE 3 (DEPENDENT VARIABLE) = PROPORTION SOOTHED
EQUATION FITTED IS Y = A0 + A1*X + A2*X**2

NO. OF INDEPENDENT VARIABLES 2 NO. OF OBSERVATIONS 5

VARIABLE	MEAN	STANDARD DEVIATION	CORRELATION W. DEP. VARIABLE
1	.95686400E+01	.72659910E+01	.6938
2	.13379460E+03	.15586980E+03	.5920
3	.55564000E+00	.22037340E+00	1.0000

CORRELATION BETWEEN INDEPENDENT VARIABLES

1 2 .9878

COMPONENT	SUM OF SQUARES	DEGRESS OF FREEDOM	VARIANCE	F
REGRESSION	.16341290E+00	2	.81706460E-01	5.30
RESIDUAL	.30844930E-01	2	.15422460E-01	
TOTAL	.19425790E+00	4	.48564460E-01	

VARIABLE	REGRESSION COEFFICIENT	VARIANCE
0	-.21486820E-01	.40927660E-01
1	.13649690E+00	.30141790E-02
2	-.54483650E-02	.65499080E-05

THE SQUARE OF THE MULTIPLE CORRELATION COEFFICIENT = .84122

INDEPENDENT VARIABLE	DEPENDENT VARIABLE		DIFFERENCE	PCT. ERR.
	OBSERVED	CALCULATED		
2.25000	.25000	.25805	.00805	.3119101E+01
4.20000	.40000	.45569	.05569	.1222119E+02
6.92310	.76920	.66236	-.10684	-.1613051E+02
15.77780	.66670	.77582	.10912	.1406546E+02
18.69230	.69230	.62628	-.06602	-.1054099E+02

APPENDIX F

RAW DATA

DEFINITION OF COLUMN HEADS

AFTER BANDAID: 30-second interval beginning after applying bandaid.

AGE: Age in months.

ANGER: Facial expression same as physical distress expression except eyes kept opened.

BEFORE BANDAID: Interval ending at time of applying bandaid.

CODE: First and last initials of subject's name; number is age.

IM: Vaccines: DTP - diphtheria, tetanus, pertussis; MMR - measles, mumps, rubella; HIB - Haemophilus influenzae type B; number after DTP indicates specific vaccine in series.

MIN: Minimum oxygen saturation.

OXYGEN SATURATION AT TIN: Minimum oxygen saturation at "in" time.

OXYGEN SATURATION AT TMAX: Minimum oxygen saturation at time of maximum fractional increase in heart rate.

OXYGEN SATURATION AT TS: Minimum oxygen saturation at soothing time.

PH: Pain history score; H indicates subject was hospitalized.

PHYSICAL DISTRESS (PAIN): Facial expression of lowered brows expression drawn together; bulging, vertical furrows in forehead between brows; broadened and bulging nasal root; fissured, tightly closed eyes; and angular, squarish mouth.

RACE: W - white; H - hispanic; B - black; O - oriental.

Rmax: maximum fractional increase in heart rate - the maximum heart rate minus the baseline heart rate divided by the baseline heart rate or, if the decimal value is multiplied by 100, the percent increase in the baseline heart rate.

SEX: F - female; M - male.

SHOTS: SS - single injection; TW - two injections.

SOOTHE: Y - yes or N - no; S - soothed or NS - not soothed; cessation of crying for at least a 10-second interval followed by no return of extended crying within 3 minutes.

Tic: time in seconds to initial cry.

TMIN: Time in seconds to minimum oxygen saturation.

Ts: soothing time - time in seconds until soothing occurred.

Tps: time to pulse soothing - the time in seconds until heart rate returned to baseline value within three minutes.

Tmax: time to maximum heart rate.

NORMALIZED HEART RATE VS TIME

TIME SEC.	LOWER LIMIT	MEAN	UPPER LIMIT
0	0.7877170	1.002658	1.217599
5	0.7965386	1.021092	1.245646
10	0.7868512	1.032610	1.278368
15	0.7506274	1.033888	1.317150
20	0.7122507	1.044612	1.376973
25	0.7405744	1.081181	1.421788
30	0.7587745	1.114302	1.469829
35	0.7600616	1.126423	1.492785
40	0.7772704	1.119335	1.461399
45	0.8254985	1.123629	1.421759
50	0.8367098	1.127000	1.417291
55	0.8130155	1.118039	1.423062
60	0.8118318	1.102825	1.393818
65	0.8083383	1.091408	1.374477
70	0.8055598	1.087421	1.369283
75	0.8067746	1.083412	1.360049
80	0.8264902	1.083921	1.341352
85	0.8385697	1.081100	1.323631
90	0.8282699	1.068833	1.309396
95	0.8231645	1.064066	1.304967
100	0.8080471	1.060998	1.313949
105	0.8061332	1.058095	1.310056
110	0.8061873	1.051494	1.296801
115	0.7987942	1.045818	1.292841
120	0.7978583	1.036340	1.274822
125	0.8019446	1.025844	1.249744
130	0.7993096	1.021062	1.242814
135	0.8052129	1.021685	1.238157
140	0.7918648	1.024342	1.256920
145	0.7885250	1.020975	1.253425
150	0.8093976	1.020710	1.232022
155	0.8232164	1.024023	1.224830
160	0.8147671	1.024216	1.233664
165	0.8005587	1.018625	1.236692
170	0.7948187	1.012119	1.229420
175	0.8007096	1.007487	1.214066
180	0.8120336	1.005625	1.199216

PAIN HISTORY, CRY, HEART RATE, AND SOOTHE DATA

CODE	RACE	SEX	IM	PH	Tic	Ts	Tps	Tmax	Rmax	SOOTHE
WC2	W	F	DTP1	4		180+	180+	42.0	0.5103	N
MK2	W	F	DTP1	8	2.11	180+	180+	49.0	0.2853	N
CV2	H	F	DTP1	5	4.57	180+	180+	42.68	0.6116	N
US2	W	F	DTP1	3	1.30	180+	180+	90.34	0.1824	N
SP2	W	F	DTP1	8	2.10	83.1	180+	72.60	0.3401	Y
JJ2	B	M	DTP1	8	1.74	180+	180+			N
MF2	W	M	DTP1	5		180+	180+	88.5	0.1285	N
KC2	B	F	DTP1	4	0.78	94.5	112.37	86.5	0.1585	Y
PC2	W	F	DTP1	5		186.0	210.33	42.0	0.1364	N
JM2	W	M	DTP1	3	1.13	93.89	101.18	30.89	0.2153	Y
AT2	B	M	DTP1	6	0.90	123.5	130.8	34.50	0.2188	Y
JO2	B	M	DTP1	5	1.76	62.66	136.21	38.66	0.2604	Y
RC2	H	M	DTP1	5	1.54	111.1	126.59	68.1	0.2883	Y
NG2	W	M	DTP1	4	1.23	60.6	82.2	71.6	0.2080	Y
CR3	W	M	DTP1	9		180+	180+	146.71	0.3462	N
AG3	B	M	DTP1	7	1.80	119.37	180+	40.37	0.2922	Y
SS3	O	F	DTP1	5	1.10	180+	180+	82.00	0.2475	N
AS4	W	F	DTP2	4	4.82	107.52	169.04	58.02	0.1081	Y
LH4	W	F	DTP2	9	4.82	60.83	180+	56.4	0.3309	Y
CO4	B	F	DTP2	5	3.31	9.75	41.67	21.75	0.0576	Y
GH4	B	F	DTP2	7		180+	180+	63.50	0.1903	N
VR4	W	M	DTP2	8		180+	180+	50.5	0.2324	N
JP4	W	M	DTP2	8	2.0	43.9	93.42	55.9	0.2254	Y
ML4	B	M	DTP2	4	3.30	180+	180+	50.0	0.2555	N

CODE	RACE	SEX	IM	PH	Tic	Ts	Tps	Tmax	Rmax	SOOTHE
NR4	W	F	DTP2	6	2.87	78.46	132.76	70.46	0.1190	Y
RA4	B	M	DTP2	6	0.95	201.9	243.17	47.90	0.5886	N
AC4	W	F	DTP2	4	3.11	64.5	180+	43.94	0.1729	Y
JS4	W	M	DTP2	6,H	1.1	180+	180+	83.10	0.1695	N
DC5	W	F	DTP2		3.30	180+	180+	47.6	0.2282	Y
JT5	W	F	DTP2	6,H	1.77	180+	180+	31.67	0.4381	N
BN5	W	M	DTP2	5	1.90	75.90	Lost monitor			Y
JM5	W	M	MMR		1.50	45.0	81.23	29.0	0.2429	Y
DM5	H	M	DTP2		3.01	199.36		19.36	0.1613	N
DL6	B	M	DTP3	6		166.20	184.70	35.7	0.6882	Y
NH6	W	M	DTP3	7	2.25	45.05	58.91	7.55	0.0447	Y
CJ6	W	F	DTP2	7	4.21	87.86	147.12	32.76	0.2868	Y
WK6	W	M	DTP2	10,H	2.98	148.83	180+	51.33	0.2937	Y
LV6	B	F	DTP3	3	1.83	102.3	133.34	50.30	0.2162	Y
BE6	B	M	DTP3	8	1.35	180+	180+	70.45	0.4048	N
TI6	W	F	DTP3	11	4.41	57.25	180+	33.25	0.2993	Y
DH6	W	M	DTP3	7	0.70	60.2	128.8	42.20	0.1655	Y
TH6	W	F	DTP3	10	1.73	180+	180+	72.00	0.1667	N
JB6	W	M	DTP3	5		128.5	173.46	37.50	0.3280	Y
HS6	W	F	DTP3	6	1.0	69.6	82.86	71.60	0.0861	Y
SB6	H	F	MMR	8	3.02	158.32	49.32	8.32	0.1591	Y
VM6	W	F	DTP1	13	2.12	138.8	159.39	11.72	0.0377	Y
SB6	W	F	DTP3	7	3.08	22.88	34.83	30.88	0.04878	Y
JH7	W	F	DTP2	4,H	1.70	180+	180+	58.6	0.1712	N
DL7	W	F	DTP2	4	1.03	180+	180+	30.44	0.2069	N
AM7	W	F	DTP3	8	3.64	71.5	111.09	35.50	0.1644	Y
CO7	W	M	DTP2	Did not cry		0.0	17.13	9.89	0.0963	Y
RM7	W	M	DTP3	6	1.67	93.33	119.84	42.33	0.1691	Y
SB8	W	F	DTP1	11		76.2	109.7	43.7	0.1181	Y

CODE	RACE	SEX	IM	PH	Tic	Ts	Tps	Tmax	Rmax	SOOTHE
JH8	W	F	DTP2	10,H	0.97	98.20	180+	25.7	0.2297	Y
CB8	W	F	DTP2	8	0.71	101.39	180+	48.88	0.1688	Y
MM8	B	F	DTP2	6		180+	180+	42.0	0.4615	N
BL8	W	F	DTP3	9	2.96	61.86	139.0	50.86	0.2632	Y
HC8	W	F	DTP3	10	3.18	123.8	169.03	38.80	0.03623	Y
MR8	W	M	DTP3	6	3.00	73.17	180+	32.07	0.3902	Y
SL8	B	F	DTP3	3	1.94	93.74	95.49	57.74	0.2928	Y
CC15	W	F	MMR	10		27.02	0.72	46.99	0.2766	Y
MW15	B	F	MMR	8	2.93	50.93	119.50	27.93	0.4000	Y
JW15	B	M	MMR	7		38.00	75.22	42.00	0.2490	Y
BW15	W	M	MMR	18	Did not cry		78.00	48.00	0.0702	Y
MJ15	B	M	MMR	6		90.08	94.33	32.08	0.4333	Y
DS15										
1st	B	F	MMR	3	2.18					
2nd*			DTP2			73.50	94.13	27.0	0.4319	Y
						46.50	67.13			
DMC15										
1st	W	M	MMR	4	1.03	Monitor lost after 140 sec.				
2nd			DTP2			129.16		84.13	0.2756	Y
						84.51		41. 51		
JS15	W	F	MMR	6	1.42	161.0	165.81	51.57	0.2742	Y
AR15	W	F	MMR	5	2.25	135.25	180+	72.25	0.2787	Y
LD15	W	F	MMR	6		140.0				Y
AJ15	W	F	MMR	10	2.30	87.5	180+	36.50	0.4335	Y

*For second injection, first calculations are from "in" time of injection #1; second calculations are from "in" time of injection #2.

CODE	RACE	SEX	IM	PH	Tic	Ts	Tps	Tmax	Rmax	SOOTHE
AP16										
1st	W	F	MMR	3	2.77					Y
2nd			DTP2			96.66	116.47	65.16	0.2266	
						63.63	83.17	31.86		
CS16	W	M	MMR	8		180+	180+	25.00	0.1739	N
LR16	W	F	MMR	8		58.97	60.05	38.97	0.1420	Y
JH16	W	M	MMR			78.88	103.54			Y
BH16	W	M	MMR	25	1.13	180+	180+	59.33	0.1574	N
CW17	W	F	MMR	6	3.32	27.73	59.80	30.82	0.1679	Y
JM17										
1st	W	M	MMR	9	3.06	9.53		48.53	0.0690	Y
2nd			DTP3		1.00	163.53	171.7			
						130.5	138.67	15.5		
KC17	W	F	MMR	6	3.40	61.9	76.13	60.9	0.1575	Y
JW17	W	M	MMR	13		180+	180+	45.7	0.4628	N
DC18	O	F	DTP3	3		180+	180+	26.5	0.8443	N
MT18	B	F	DTP4	4	2.20	50.7	180+			Y
ST18										
1st	W	F	HIB	4	1.89	13.5		67.8		
2nd			DTP4		0.77	110.35	160.35	27.9	0.6449	Y
						70.40	120.4			
KD18										
1st	W	M	HIB	13 H	0.5			46.4		Y
2nd			DTP4			81.4	105.4	13.54	0.1812	
						48.54	72.54			

CODE	RACE	SEX	IM	PH	Tic	Ts	Tps	Tmax	Rmax	SOOTHE
WG18										
1st	W	M	MMR	8	1.13					Y
2nd			DTP4			113.33	108.00	40.33	0.4750	
						81.10	85.77			
NB18	W	F	HIB	12		72.58	126.54	94.8	0.4048	Y
MM18	W	M	MMR	7	2.49	11.09	33.59	16.09	0.1083	Y
KS18										
1st	W	F	MMR	10						N
2nd			DTP4			180+	180+	55.0	0.3556	
SK18										
1st	W	F	MMR	5	Did not cry					
2nd			DTP4		0.40	25.5	180+	44.9	0.2458	Y
NK18	W	M	DTP4	7,H	2.20	40.1	46.33	19.1	0.1810	Y
DB18										
1st	W	M	HIB	11				45.0	0.2797	N
2nd			DTP4			180+	180+			
ZG18										
1st	W	M	MMR	8	1.19			67.67	0.0483	Y
2nd			DTP4			115.67	201.83			
						52	58.16			
AMC19	W	F	HIB	Cried all the way; lost monitor						N
			DTP4							
AR19	W	F	DTP4	8	0.97	37.71	66.43	36.63	0.4661	Y
JJ19										
1st	W	M	HIB	5	Cried all the way			42.08		N
2nd			DTP?	Not soothed						

CODE	RACE	SEX	IM	PH	Tic	Ts	Tps	Tmax	Rmax	SOOTHE
NG19	W	M	MML	10		85.5	Lost monitor			Y
SR19										
1st	W	M	MMR	14						
2nd			DTP3			129.0	163.26	25.0	0.2927	Y
RM19	H	M	HIB	Cried all the way				86.0	0.0867	N
			DTP3	Not soothed						
PP20	W	F	MMR	5,H	2.45	180+	180+	74.0	0.5046	N
AP20										
1st	H	F	HIB	6	0.3	98.2	138.44	63.2	0.0822	Y
2nd			DTP3			65.5	105.74			
BH21	W	M	DTP3	8	0.1	10	180+	31.0	0.2986	Y

c:code1.dis

CODE TABLE FOR OXYGEN SATURATION RATE

CODE	AGE	PH	TMIN	MIN	OXYGEN SATURATION AT TIN	AT TMAX	AT TS	SHOTS	SOOTHE	RACE	SEX
WC2	2.0	4.0	22.00	94.	97.	100.	0.	SS	NS	W	F
MK2	2.0	8.0	20.00	92.	100.	100.	0.	SS	NS	W	F
CV2	2.0	5.0	67.68	81.	100.	100.	0.	SS	NS	H	F
US2	2.0	3.0	35.00	95.	99.	98.	0.	SS	NS	W	F
SP2	2.0	8.0	10.60	81.	98.	100.	100.	SS	S	W	F
JJ2	2.0	8.0	.00	0.	65.	0.	0.	SS	NS	B	M
MF2	2.0	5.0	68.50	80.	85.	93.	0.	SS	NS	W	M
KC2	2.0	4.0	21.50	84.	100.	98.	96.	SS	S	B	F
PC2	2.0	5.0	17.00	88.	97.	100.	0.	SS	NS	W	F
JM2	2.0	3.0	100.89	94.	97.	99.	97.	SS	S	W	M
AT2	2.0	6.0	119.50	95.	97.	100.	100.	SS	S	B	M
JO2	2.0	5.0	73.66	41.	88.	96.	100.	SS	S	B	M
RC2	2.0	5.0	98.10	87.	98.	99.	97.	SS	S	H	M
NG2	2.0	4.0	11.60	91.	98.	97.	97.	SS	S	W	M
CR3	3.0	9.0	30.00	80.	99.	95.	0.	SS	NS	W	M
AG3	3.0	7.0	160.37	60.	93.	97.	77.	SS	S	B	M
SS3	3.0	5.0	122.00	85.	100.	99.	0.	SS	NS	O	F
MR4	4.0	5.0	55.00	95.	100.	98.	98.	SS	S	H	F
AS4	4.0	4.0	3.02	65.	92.	83.	88.	SS	S	W	F
LH4	4.0	9.0	56.40	98.	100.	98.	99.	SS	S	W	F
CO4	4.0	5.0	3.31	93.	100.	93.	93.	SS	S	B	F
GH4	4.0	7.0	.00	0.	0.	0.	0.	SS	NS	B	F
VR4	4.0	8.0	8.50	93.	100.	98.	0.	SS	NS	W	M
JP4	4.0	8.0	50.90	85.	99.	92.	89.	SS	S	W	M
ML4	4.0	4.0	70.00	89.	0.	100.	0.	SS	NS	B	M
NR4	4.0	6.0	45.46	85.	100.	97.	94.	SS	S	W	F
RA4	4.0	6.0	92.90	68.	100.	100.	0.	SS	NS	B	M
AC4	4.0	4.0	29.50	98.	100.	100.	100.	SS	S	W	F
JS4	4.0	.0	46.10	93.	98.	98.	0.	SS	NS	W	M
DC5	5.0	.0	55.00	93.	99.	95.	97.	SS	S	W	F
JT5	5.0	.0	115.00	92.	99.	99.	0.	SS	NS	W	F
BN5	5.0	5.0	.00	0.	0.	0.	0.	SS	S	W	M
JM5	5.0	.0	119.00	91.	99.	96.	100.	SS	S	W	M
DM5	5.0	.0	5.96	82.	90.	94.	0.	SS	NS	H	M
DL6	6.0	6.0	70.00	98.	100.	100.	100.	SS	S	B	M
NH6	6.0	7.0	10.00	74.	93.	79.	96.	SS	S	W	M
CJ6	6.0	7.0	27.58	90.	98.	91.	99.	SS	S	W	F
WK6	6.0	.0	25.00	61.	100.	93.	95.	SS	S	W	M
LV6	6.0	3.0	50.30	92.	99.	92.	100.	SS	S	B	F
BE6	6.0	8.0	110.45	98.	100.	99.	0.	SS	NS	B	M
TI6	6.0	11.0	23.25	97.	99.	97.	99.	SS	S	W	F
DH6	6.0	7.0	27.20	66.	98.	98.	100.	SS	S	W	M
TH6	6.0	10.0	22.00	83.	99.	96.	0.	SS	NS	W	F
JB6	6.0	5.0	7.50	77.	93.	100.	100.	SS	S	W	M
HS6	6.0	6.0	31.60	85.	99.	96.	96.	SS	S	W	F
SB6	6.0	8.0	18.32	90.	100.	96.	100.	SS	S	H	F
VM6	6.0	.0	21.72	88.	99.	93.	99.	SS	S	W	F
SB6	6.0	7.0	.00	0.	97.	98.	98.	SS	S	W	F
JH7	7.0	.0	83.60	93.	100.	96.	0.	SS	NS	W	F
DL7	7.0	4.0	25.44	92.	100.	99.	0.	SS	NS	W	F
AM7	7.0	8.0	40.40	96.	100.	99.	99.	SS	S	W	F
CO7	7.0	.0	9.89	99.	100.	99.	100.	SS	S	W	M
RM7	7.0	6.0	42.93	93.	98.	93.	99.	SS	S	W	M

CODE TABLE FOR OXYGEN SATURATION RATE (COT.TXT)

CODE	AGE	PH	TMIN	MIN	OXYGEN SATURATION AT TIN	AT TMAX	AT TS	SHOTS	SOOTHE	RACE	SEX
SB8	8.0	11.0	23.70	82.	98.	98.	100.	SS	S	W	F
JH8	8.0	.0	15.70	89.	98.	99.	99.	SS	S	W	F
CB8	8.0	8.0	33.88	88.	93.	98.	91.	SS	S	W	F
MM8	8.0	6.0	12.00	96.	95.	100.	0.	SS	NS	B	F
BL8	8.0	9.0	35.86	96.	100.	98.	99.	SS	S	W	F
HC8	8.0	10.0	48.80	94.	100.	100.	100.	SS	S	W	F
MR8	8.0	6.0	37.07	96.	98.	98.	98.	SS	S	W	M
SL8	8.0	3.0	72.74	56.	99.	96.	99.	SS	S	B	F
CC15	15.0	10.0	55.00	98.	98.	100.	99.	SS	S	W	F
MW15	15.0	8.0	27.93	93.	100.	93.	100.	SS	S	B	F
JW15	15.0	7.0	42.00	96.	99.	96.	98.	SS	S	B	M
BW15	15.0	18.0	.00	0.	99.	99.	99.	SS	S	W	M
MJ15	15.0	6.0	12.08	97.	100.	99.	100.	SS	S	B	M
DS15	15.0	3.0	27.00	97.	100.	97.	100.	TS	S	B	F
DMC15	15.0	4.0	34.13	27.	98.	97.	97.	TS	S	W	M
JS15	15.0	6.0	40.00	76.	99.	98.	98.	SS	S	W	F
AR15	15.0	5.0	27.25	88.	100.	98.	100.	SS	S	W	F
LD15	15.0	6.0	.00	0.	92.	100.	100.	SS	S	W	F
AJ15	15.0	10.0	21.50	89.	98.	97.	99.	SS	S	W	F
AP16	16.0	3.0	23.12	97.	100.	99.	100.	TS	S	W	F
CS16	16.0	8.0	13.34	90.	99.	99.	0.	SS	NS	W	M
LR16	16.0	8.0	23.97	95.	100.	98.	97.	SS	S	W	F
JH16	16.0	.0	16.88	92.	99.	98.	97.	SS	S	W	M
BH16	16.0	25.0	59.33	92.	97.	92.	0.	SS	NS	W	M
CW17	17.0	6.0	30.82	80.	100.	92.	92.	SS	S	W	F
JM17	17.0	9.0	83.53	97.	99.	97.	99.	TS	S	W	M
KC17	17.0	6.0	35.90	95.	99.	95.	95.	SS	S	W	F
JW17	17.0	13.0	.00	0.	0.	0.	0.	SS	NS	W	M
DC18	18.0	3.0	101.50	83.	95.	98.	0.	SS	NS	O	F
MT18	18.0	4.0	.00	0.	0.	0.	100.	SS	S	B	F
ST18	18.0	4.0	72.85	96.	100.	97.	98.	TS	S	W	F
KD18	18.0	.0	51.40	65.	100.	66.	99.	TS	S	W	M
WG18	18.0	8.0	65.33	90.	99.	95.	100.	TS	S	W	M
NB18	18.0	12.0	34.48	92.	94.	95.	98.	SS	S	W	F
MM18	18.0	7.0	18.09	97.	99.	99.	98.	SS	S	W	M
KS18	18.0	10.0	20.00	86.	92.	98.	0.	TS	NS	W	F
SK18	18.0	5.0	.00	0.	98.	99.	99.	TS	S	W	F
NK18	18.0	.0	10.69	92.	98.	93.	98.	SS	S	W	M
DB18	18.0	11.0	15.00	49.	65.	99.	0.	TS	NS	W	M
ZG18	18.0	8.0	67.67	95.	98.	99.	99.	TS	S	W	M
AMC19	19.0	9.0	.00	0.	0.	0.	0.	SS	NS	W	F
AR19	19.0	8.0	31.63	98.	99.	99.	99.	SS	S	W	F
JJ19	19.0	5.0	22.08	92.	99.	92.	0.	TS	NS	W	M
NG19	19.0	10.0	.00	0.	0.	0.	0.	SS	S	W	M
SR19	19.0	14.0	.00	93.	99.	99.	99.	TS	S	W	M
RM19	19.0	.0	86.00	90.	100.	90.	0.	SS	NS	H	M
PP20	20.0	.0	40.00	67.	97.	95.	0.	SS	NS	W	F
AP20	20.0	6.0	6.00	92.	100.	98.	99.	TS	S	H	F
BH21	21.0	8.0	3.50	95.	99.	98.	98.	SS	S	W	M

PROPORTION OF PHYSICAL DISTRESS FACE(PAIN)
AND ANGER FACE BEFORE AND AFTER BANDAID

					FACIAL EXPRESSION			
					BEFORE BANDAID		AFTER BANDAID	
CODE	RACE	SEX	IM	PH	PAIN FACE	ANGER FACE	PAIN FACE	ANGER FACE
WC-2	W	F	DPT1	4	1.0	0.0	1.0	0.0
MK-2	W	F	DPT1	8	1.0	0.0	1.0	0.0
CV-2	H	F	DPT1	5	1.0	0.0	1.0	0.0
US-2	W	F	DPT1	3	1.0	0.0	1.0	0.0
SP-2	W	F	DPT1	8	1.0	0.0	1.0	0.0
JJ-2	B	M	DPT1	8	1.0	0.0		
MF-2	W	M	DPT1	5	1.0	0.0	1.0	0.0
KC-2	B	F	DPT1	4	1.0	0.0	0.75	0.25
PC-2	W	F	DPT1	5	0.765	0.235	0.0	1.0
JM-2	W	M	DPT1	3	1.0	0.0	0.51	0.49
AT-2	B	M	DPT1	6	1.0	0.0	0.857	0.143
JO-2	B	M	DPT1	5	1.0	0.0	0.345	0.655
RC-2	H	M	DPT1	5	1.0	0.0	1.0	0.0
NG-2	W	M	DPT1	4	1.0	0.0	1.0	0.0
CR-3	W	M	DPT1	9	1.0	0.0	1.0	0.0
AG-3	B	M	DPT1	7	1.0	0.0	1.0	0.0
SS-3	O	F	DPT1	5	1.0	0.0	1.0	0.0
ED-4	W	M	DPT1	7	0.785	0.215	0.797	0.203
MR-4	H	F	DPT2	5	1.0	0.0	0.348	0.652
AS-4	W	F	DPT2	4	1.0	0.0	1.0	0.0
LH-4	W	F	DPT2	9	1.0	0.0	0.684	0.316
CO-4	B	F	DPT2	5	0.909	0.091	0.0	1.0
GM-4	B	F	DPT2	7	1.0	0.0	1.0	0.0
JP-4	W	M	DPT2	8	1.0	0.0	0.78	0.22
ML-4	B	M	DPT2	4	1.0	0.0		
NR-4	W	F	DPT2	6	1.0	0.0	1.0	0.0
RA-4	B	M	DPT2	6	1.0	0.0	0.848	0.152
AC-4	W	F	DPT1	4	1.0	0.0	0.63	0.37
JS-4	W	M	DPT2	6,H	1.0	0.0	1.0	0.0
VR-4	W	M	DPT2	8	1.0	0.0	0.688	0.312
DC-5	W	F			1.0	0.0	0.574	0.426
JJ-5	W	F	DPT2	6,H	1.0	0.0		
BN-5	W	M	DPT2	5	1.0	0.0	0.677	0.323
JM-5	W	M	MMR		1.0	0.0	0.0	1.0
DM-5	H	M	DPT2		1.0	0.0	0.398	0.602
DL-6	B	M	DPT3	6	1.0	0.0	0.821	0.179
NH-6	W	M	DPT3	7	1.0	0.0	0.531	0.469
CT-6	W	F	DPT2	7	1.0	0.0		
WK-6	W	M	DPT2	10,H	1.0	0.0	1.0	0.0
LW-6	B	F	DPT3	3	0.0	1.0	0.0	1.0
BE-6	B	M	DPT3	8	1.0	0.0	0.318	0.767
TI-6	W	F	DPT3	11	1.0	0.0	0.233	0.767
DH-6	W	M	DPT3	7	1.0	0.0	0.259	0.741
TH-6	W	F	DPT3	10	1.0	0.0	0.5	0.5
JB-6	W	M	DPT3	5	0.0	1.0	0.0	1.0
MS-6	W	F	DPT3	6	1.0	0.0	1.0	0.0
SB-6	H	F	MMR	8	1.0	0.0	0.5	0.5

					FACIAL EXPRESSION			
					BEFORE BANDAID		AFTER BANDAID	
CODE	RACE	SEX	IM	PH	PAIN FACE	ANGER FACE	PAIN FACE	ANGER FACE
VM-6	W	F	DPT1	13,H	1.0	0.0	0.636	0.364
SB-6	W	F	DPT3	7	0.0	1.0	0.0	1.0
JH-7	W	F	DPT2	9,H	1.0	0.0	0.336	0.664
DL-7	W	F	DPT2	4	1.0	0.0	0.231	0.769
AM-7	W	F	DPT3	8	1.0	0.0	0.434	0.566
CO-7	W	M	DPT2		DID NOT CRY			
RM-7	W	M	DPT3	6	1.0	0.0	0.474	0.526
CC-15	W	F	MMR	10	1.0	0.0	0.259	0.741
MM-15	H	F	MMR	8	1.0	0.0	0.0	1.0
JW-15	B	M	MMR	7	1.0	0.0		
MJ-15	B	M	MMR	6	1.0	0.0	0.851	0.149
DS-15	B	M	MMR	3	1.0	0.0	0.419	0.581
			DPT2	3	0.25	0.75	0.0	1.0
DMC-15	W	M	MMR	4	0.0	1.0		
			DPT2	4	0.473	0.527	0.0	1.0
JS-15	W	F	MMR	6	1.0	0.0		
AR-15	W	F	MMR	5	1.0	0.0	0.0	1.0
LO-15	W	F	MMR	6	0.0	1.0	0.0	1.0
AJ-15	W	F	MMR	10	1.0	0.0	0.0	1.0
CI-15	B	F	MMR	3	0.0	1.0	0.0	1.0
KB-15	W	M	MMR	14,H	1.0	0.0	0.265	0.735
BW-15	W	M	MMR		DID NOT CRY			
AP-16	W	F	MMR	3	1.0	0.0	0.722	0.278
			DPT2	3			0.0	1.0
CS-16	W	M	MMR	8	0.0	1.0	0.0	1.0
LR-16	H	F	MMR	8	1.0	0.0	0.808	0.192
JH-16	W	M	MMR		0.0	1.0	0.0	1.0
BH-16	W	M	MMR	25	0.0	1.0	0.0	1.0
CW-17	W	F	MMR	6	1.0	0.0	0.0	1.0
JM-17	W	M	MMR	9	0.0	1.0		
			DPT3	9	1.0	0.0	0.0	1.0
KC-17	W	F	MMR	6	1.0	0.0	0.2	0.8
JW-15	W	M	MMR	13	1.0	0.0	0.138	0.862
DC-18	O	F	DPT3	3	0.704	0.296	0.698	0.302
MT-18	B	F	DPT4	4	1.0	0.0	0.0	1.0
KD-18	W	M	HIB	13,H	1.0	0.0	0.346	0.654
				13,H	0.0	1.0	0.0	1.0
WG-18	W	M	MMR	8	1.0	0.0	0.0	1.0
			DPT4	8	0.788	0.222	0.0	1.0
NB-18	W	F	HIB	12	1.0	0.0		
MM-18	W	M	MMR	7	1.0	0.0		
KS-18	W	F	MMR	10	1.0	0.0		
			DPT4	10	0.0	1.0	0.0	1.0
KS-18	W	F	MMR	5	DID NOT CRY FOR IST SHOT			
			DPT4	5	0.886	0.114		
NK-18	W	M	DPT4	7,H	0.0	1.0		
DB-18	W	M	MMR	11	1.0	0.0	1.0	0.0
			DPT4	11	1.0	0.0	0.697	0.303

					FACIAL EXPRESSION			
					BEFORE BANDAID		AFTER BANDAID	
CODE	RACE	SEX	IM	PH	PAIN FACE	ANGER FACE	PAIN FACE	ANGER FACE
ZG-18	W	M	MMR	8	1.0	0.0	1.0	0.0
			DPT4	8	0.722	0.278	0.0	1.0
ST-18	W	F	HIB	4	0.882	0.118	0.0	1.0
			DPT4	4	1.0	0.0	0.0	1.0
AMC-19	W	F	HIB	9				
			DPT4	9				
AR-19	W	F	DPT4	8			0.833	0.167
JJ-19	W	M	HIB	5	0.0	1.0	0.0	1.0
			DPT4	5	0.0	1.0	0.0	1.0
NG-19	W	F	MMR	10	1.0	0.0	0.0	1.0
SR-19	W	M	MMR	14	1.0	0.0	0.0	1.0
			DPT3	14	1.0	0.0	0.0	1.0
RM-19	H	M	HIB		0.0	1.0	0.0	1.0
			DPT3		0.0	1.0	0.0	1.0
PP-20	W	F	MMR	5,H	1.0	0.0	0.741	0.259
AP-20	H	F	HIB	6	0.0	1.0	0.0	1.0
			DPT3	6	0.0	1.0	0.0	1.0
BH-21	W	M	DPT3	8	1.0	0.0	0.0	1.0

VITA

Donna L. Wong

Candidate for the Degree of

Doctor of Philosophy

Thesis: PHYSIOLOGICAL RESPONSES, FACIAL EXPRESSIONS, AND CRY OF INFANTS DURING IMMUNIZATION IN RELATION TO THEIR PAIN HISTORY

Major Field: Home Economics

Area of Specialization: Child Development

Biographical:

Personal Data: Born in Passaic, New Jersey, March 30, 1948, the daughter of Rudolph and Madeline Mitchko.

Education: Graduated from St. Bonaventure High School, Paterson, New Jersey, in June 1966; received Bachelor of Science Degree in Nursing from Rutgers, The State University at Newark, New Jersey in 1970; received Masters of Nursing Degree from University of California at Los Angeles in 1971; completed requirements for the Doctor of Philosophy degree at Oklahoma State University in December, 1992.

Professional Experience: Charge Nurse, Pediatrics, University of California Medical Center, Los Angeles, 1979-1971; Pediatric Clinical Specialist, Roosevelt Hospital, New York, 1972-1973; Assistant Professor, Nursing of Children, Seton Hall University, New Jersey, 1973-1977, Nurse Counselor in Private Practice, 1975-Present; Guest Lecturer, Nursing of Children, oral Roberts University Graduate School of Nursing, Oklahoma, Fall 1983; Pediatric Nurse Consultant, Westchester County Medical Center, New York, 1976; Muhlenberg Hospital, New Jersey, 1976-1980, Somerset Medical Center, New Jersey, 1977-1980, St. Joseph's Medical Center, New Jersey, 1979-1980, Hillcrest Medical Center, Oklahoma, 1981-1983, Arkansas Children's Hospital, 1987-1991, Saint Francis Hospital Children's Center, Oklahoma, 1987-Present, Children's Medical Center of Dallas, Texas, 1990-Present; Adjunct Associate Professor, University of Oklahoma College of Medicine-Tulsa, 1991-Present.

Scholarly Activities: More than 60 publications, including articles, chapters in books, and 3 major pediatric nursing textbooks through 4 editions (6 refereed publications are on pain in children); more than 180 invited presentations (44 on pain in children); member of 16 professional organizations, including International Association for the Study of Pain; American Pain Society; Sigma Theta Tau (Zeta Delta Chapter), Honorary Nursing Society; Omicron Nu (Xi Chapter), Home Economics National Honor Society; Fellow of American Academy of Nursing; listed in Who's Who in Nursing.

Received the following awards:
Ella V. Stonsby Award, Rutgers University College of Nursing, Highest Scholastic Achievement, 1970.
Magna Cum Laude, Rutgers University, 1970.
Magna Cum Laude, University of California, 1971.
Outstanding Educator of America Award, 1974-1975.
Burns Pioneer Award, National Burn Victim Foundation, 1977.
American Journal of Nursing Book of the Year Award, 1980, 1982, 1983, 1984, 1985, 1986, 1987, 1990, and 1992.
Outstanding Service Award, American Cancer Society, 1980.
Honorary Recognition Award, Oklahoma Nurses Association, 1987.
Pediatric Nursing Book Award, 1988, 1989, 1991.
Excellence in Research Award, Zeta Delta Chapter of Sigma Theta Tau, 1988.
National Association of Pediatric Nurse Associates and Practitioners (NAPNAP) Henry K. Silver Award, 1991.
Fellow, American Academy of Nursing, 1991.
Writer's Award, Pediatric Nursing, 1991.
Outstanding Service Award, Oklahoma NAPNAP, 1992.

Received the following fellowships and grants:
DHEW Traineeship for Graduate Study, 1970-1971.
National Association of Pediatric Nurse Associates and Practitioners (NAPNAP) Foundation Research Grant, 1985.
Oklahoma Nurses Foundation Small Grant Awards, 1985, 1991.
Oklahoma State University Karl and Louise Wolf Home Economics Graduate Fellowship, 1988-1989 and 1989-1990.
Sigma Theta Tau Chapter Zeta Delta Research Award, 1990.
National Association of Pediatric Nurse Associates and Practitioners (NAPNAP) Foundation Research Grant, 1991.