A Pilot Study of Milk Odor Effect on Nonnutritive Sucking by Premature Newborns

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**Objective:** To study the effect of milk odor on nonnutritive sucking by premature newborns.

**Design:** Blinded, crossover study of the effects of milk vs sham odor on nonnutritive sucking.

**Setting:** Urban neonatal intensive care unit.

**Patients:** Twenty-nine premature newborns with gestational age of 29 to 36 weeks.

**Intervention:** Fourteen subjects were tested with fortified breast milk odor (group 1) and 15 were tested with formula odor (group 2). For the test observation, milk odor was directed to the nose (orthonasal exposure) using a specially modified pacifier. For the control observation, water was used as a sham odor. Observations were made concurrently with tube feeding of the newborn with either fortified breast milk (group 1) or formula (group 2).

**Main Outcome Measures:** Total number of sucks and sucking bursts, measured from a digital record of pressure changes within the pacifier.

**Results:** Nutrient odor increased suck bursts in group 1 subjects, with borderline statistical significance (46.6 bursts/10 min with odor [95% confidence interval (CI), 39-54] vs 35.4 bursts/10 min without odor [95% CI, 28-43]). Unexpectedly, when test and control observations were combined, subjects in group 1 showed an overall increase in number of sucks (260.4 [95% CI, 206-315]) and suck bursts (41.0 [95% CI, 36-46]) compared with group 2 subjects (144.8 [95% CI, 87-203] vs 27.4 [95% CI, 21-34]).

**Conclusions:** Nutrient odor exposure via pacifier may stimulate nonnutritive sucking during gavage feeding of premature newborns. Further studies on the effects of nutrient odor on nonnutritive sucking by premature newborns must take into account the effects of nutrients given via gavage.

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The therapeutic value of pacifier-induced nonnutritive sucking (NNS) for newborns includes calming, analgesic effects, and promotion of weaning from gastric tube feeding. While the full impact of oral sensorimotor deprivation associated with the tube feeding of sick newborns is uncertain, it is well established that the restoration of oral-tactile stimulation via pacifier improves the oral feeding skills of tube-fed premature newborns. Pacifiers have therefore become a conventional part of the care of these patients.

Newborns’ attraction to the odor of breast milk is one of the fundamental behavioral responses that human newborns share with other mammalian species. Their ability to distinguish the odor of their mother’s breast milk from that of other mothers reflects human newborns’ exquisite olfactory sensitivity. In addition to mediating social recognition, maternally derived odors organize and stimulate newborns’ feeding behavior. This attraction has most often been measured as a tendency to turn the head toward the odor source, a response that orients the newborn’s mouth toward its food.

Studies of newborns’ behavioral responses to odors have often made note of mouthing movements or sucking behavior. Like the tactile stimulus of a pacifier, therefore, chemosensory stimuli seem to be salient sensory cues of NNS. However, few studies have formally addressed whether or how chemosensory stimuli may regulate this adaptive ingestive behavior.

Considering the positive effects of NNS for premature newborns, chemosensory augmentation of NNS may prove to be clinically useful in this population. More-
over, the association of feeding with maternally derived odor, such as breast milk odor, may have positive effects on breastfeeding independent of the odor’s effects on NNS. To assess the feasibility of controlling tube-fed newborns’ exposure to nutrient odor during gavage feeding and to obtain preliminary data on nutrient odors’ effect on NNS, we developed a method for delivering milk odor orthogonally. We then conducted a blinded, crossover study of the effect of this odor exposure on NNS in premature newborns. Twenty-nine newborns consuming either formula or fortified breast milk were studied. An operant conditioning paradigm of NNS reinforcement (milk odor exposure contingent on NNS) was used to conform to behavioral contingencies of normal newborn feeding.

**METHODS**

Twenty-nine subjects, with gestational age ranging from 29 to 36 weeks, were tested at the bedside in the neonatal intensive care nursery. All had a nasal feeding tube in place and received tube feedings concurrently with NNS observations. Subjects were excluded if they had documented neurologic disease or an anomaly of the gut, heart, or oropharynx. Procedures were approved by the institutional review boards of the Children’s Hospital of Philadelphia (Philadelphia, Pa) and Pennsylvania Hospital (Philadelphia). Written consent was obtained from the parents of all subjects.

Subjects underwent two 10-minute observations at the bedside in random order, 1 with and 1 without odor reinforcement. The 2 observation periods took place within 24 hours, and the order of odor vs no-odor reinforcement was balanced: half of the subjects were given the control stimulus (no odor) during the first observation period, and the other half of the subjects were given the control stimulus during the second observation period. Subjects were tested in an awake state, had not been fed (by tube or orally) for at least 2 hours, and had not undergone a procedure within 24 hours. During observations, the newborn remained supine, and the experimenter wore no scented substances. If present, the parents were asked to wait outside the nursery. All had a nasal feeding tube in place and were not undergone a procedure within 24 hours. Procedures were approved by the institutional review boards of the Children’s Hospital of Philadelphia (Philadelphia, Pa) and Pennsylvania Hospital (Philadelphia). Written consent was obtained from the parents of all subjects.

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The subjects were exposed to milk or sham odor contingent on sucking activity by using a pacifier adapted for this purpose. Fourteen subjects were tested with the odor of fortified breast milk (group 1), and 15 other subjects were tested with the odor of formula (group 2). For all subjects, 200 µL of milk ( fortified breast milk or formula) dropped on sterile gauze was used as the test odor, and the test odor source was the same type of milk as that given via gavage during both observations. All but 4 subjects in group 2 were given Special Care formula (Ross Products Division of Abbott Laboratories, Columbus, Ohio). Three others were given Neosure (Ross Products), and 1 was given Isomil (Mead Johnson Nutritional, Evansville, Ind.). For sham odor observations, 200 µL of sterile water for intravenous use was used as the odor source.

Breast milk was allowed to thaw in plastic freezing containers and warm to room temperature in warm tap water for about 13 to 20 minutes, after which a powdered fortifier was added according to the manufacturer’s instructions (Similac Human Milk Fortifier; Ross Products). Fortified breast milk aliquots were then taken directly using a pipette. Formula aliquots were taken directly from fresh bottles of formula at room temperature. The pacifier was prepared by an individual who was not responsible for controlling the device during the observation. Tinting of the silicone pacifier prevented the individual controlling the pacifier from discerning test (odor) vs no odor) conditions. If the newborn ejected the pacifier, a brief (5-second) attempt was made to reinsert the pacifier after 60 seconds.

The pacifiers were also instrumented with a pressure transducer so that sucking activity could be recorded directly onto a laptop computer (Figure). The pressure transducer was, in turn, connected to a laptop personal computer with a data acquisition card. Positive intraluminal pressure associated with sucking produced a signal that could be visualized on the computer. The 10-minute record of pressure changes was stored as a digital file for later, blinded assessment of NNS.

The complete data set consisted of 58 digital files (29 subjects, 2 10-minute records per subject). Sucking activity appeared as a distinct, biphasic wave lasting 0.3 to 0.5 seconds. Although some sucking waves were contaminated by artifact (mouthing of the pacifier or by airflow over the nasal cannulae apertures due to compression of the nipple and the newborn’s nostrils), they could be visually distinguished from NNS activity. A blinded reviewer therefore counted the total number of sucks and bursts by visually reviewing each record. A burst was defined as 2 or more successive sucks whose peaks were separated by no more than 1 second. To assess the reproducibility of these blinded measures, a 2-minute sample of each of 15 records was reviewed by 2 different reviewers. These independent measures were compared using the Pearson correlation coefficient.

The mean number of individual sucks and of sucking bursts with vs without milk odor reinforcement was computed for subjects in each group. The effects of other clinical and demographic variables on sucking measures were also tested using an analysis of variance.

The Wee Soothie pacifier (Children’s Medical Ventures Inc, South Weymouth, Mass) was adapted so that the newborn received an odor stimulus from cannulae mounted on the pacifier hilt in response to sucking (Figure). The pacifier could be loaded with cotton gauze (osmophore) partially saturated with a liquid odor source. The osmophore consisted of a ¼-in square of cotton gauze onto which a 200-µL aliquot of either milk (fortified breast milk or formula) or water was dropped by an automatic pipette.

Observations were made to confirm that compression of the nipple, as occurs with sucking on the nipple by a newborn, forced air to flow from the nipple lumen, through the cannulae, and toward the subject’s nose. The lumen of the pacifier was flushed with 100% carbon dioxide via a tube connecting...
to the nipple luminal space via the seal. Slight compressions of the lumen caused a phasic increase in the carbon dioxide concentration at the cannulae apertures, as measured by a carbon dioxide detector. This pattern indicated that sucking on the modified pacifier expressed gas from nasal canulae.

### RESULTS

The Pearson correlation coefficient of the independently reviewed records was 0.95 for bursts and 0.96 for sucks, indicating that sucking activity could be discerned reliably from the digital records. Demographic data and feeding history are presented in Table 1. Although they were tested with formula odor, most newborns in group 2 had received some combination of breast milk and fortified breast milk in the days prior to the observation. We therefore tabulated the total number and relative percentage of days that the newborns had been given either breast milk or fortified breast milk prior to the day of testing (Table 1). Means for all clinical and demographic descriptors were similar in both groups of newborns.

Summary statistics on sucking activity of study subjects are presented in Table 2. Ninety-five percent confidence intervals (CIs) for bursts with vs without odor reinforcement for group 1 showed a borderline increase in sucking burst activity (39-54 bursts with odor vs 28-43 bursts without odor). In a post hoc comparison, subjects fed fortified breast milk showed greater suck and suck burst measures compared with subjects fed formula (group 1: 95% CI, 36-46 bursts, 206-315 sucks; group 2: 95% CI, 21-34 bursts, 87-203 sucks). Analysis of the following variables showed no interaction with the milk odor effect on sucking and no effect on measures of sucking overall: gestational age at birth or at time of test, weight at birth or at time of test, age (in days), number or percentage of days fed breast milk, and number or percentage of maternal visit days.

### COMMENT

In light of observations that NNS has therapeutic value for tube-fed, premature newborns, we performed a pilot study on the effect of milk odor on NNS. We developed and piloted a means of delivering nutrient odors to tube-fed, premature newborns contingent on NNS behavior. Our preliminary results suggest that nutrient odor may increase NNS during tube feeding. The odor of nutrients containing human breast milk, such as fortified breast milk, may have advantages as sensory reinforcers of NNS. Unexpectedly, newborns consuming fortified breast milk via gavage showed approximately a 50% increase in sucks and in the number of sucking bursts compared with newborns consuming formula.

Some authors have suggested that gavage feeding may enhance NNS activity, but it is unclear what afferent stimuli associated with tube feeding might mediate this response. While the chemosensory sensations associated with tube feeding remain a matter of conjecture, it is possible that stimulation of retronasal olfactory epithelium during gavage feeding could positively influence digestive behavior. Subjects receiving fortified breast milk via gavage showed greater NNS activity independent of odor exposure. A possible effect of milk type on NNS during gavage feeding seen in our subjects remains to be confirmed.

Sucking measures showed no effect of odor among subjects exposed to formula odor (group 2). Further studies with a larger number of subjects will be needed to determine whether the breast milk component of fortified breast milk odor constitutes an important behavior-reinforcing stimulus of NNS. Also, future studies will benefit from methods that separate odor delivery from NNS measurement functions. The use of an olfactometer for example, would allow for controlled delivery of nutrient odor that could be coupled to NNS activity. This approach would likely improve signal-to-noise ratio and so permit the use of a computer-based algorithm for measuring NNS activity.

The measures of NNS reported here accord with previously published reports. Our preterm subjects sucked between 26 and 15 times per minute during the 10-minute observation period, while results of Maone et al reflected sucking rates between 34/min (sucrose reinforcement) and 19/min (water control). In a recent study on NNS, Lundqvist and Hafstrom found a burst duration of 2.43 to 3.56 seconds for preterm newborns of 31

### Table 1. Demographic and Clinical Characteristics of Subjects*

<table>
<thead>
<tr>
<th>Test Odor</th>
<th>Group 1 FBM</th>
<th>Group 2 Formula</th>
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</thead>
<tbody>
<tr>
<td>Gestational age at birth, wk</td>
<td>30.3 ± 2.5</td>
<td>29.3 ± 2.3</td>
</tr>
<tr>
<td>Gestational age at test, wk</td>
<td>33.8 ± 1.7</td>
<td>32.7 ± 1.7</td>
</tr>
<tr>
<td>Postnatal age at test, d</td>
<td>25.2 ± 15.3</td>
<td>23.7 ± 11.3</td>
</tr>
<tr>
<td>Birthweight, g</td>
<td>1442.1 ± 367.5</td>
<td>1372.2 ± 317.0</td>
</tr>
<tr>
<td>Race, white/black/Hispanic/Asian</td>
<td>7/7/0/0</td>
<td>2/11/1/1</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>6/8</td>
<td>7/8</td>
</tr>
<tr>
<td>Mean Apgar scores (1 min/5 min)</td>
<td>6.6/8.4</td>
<td>7.0/8.4</td>
</tr>
<tr>
<td>Maternal age, y</td>
<td>30.4 ± 6.7</td>
<td>27.3 ± 6.3</td>
</tr>
<tr>
<td>Days receiving oxygen</td>
<td>10.2 ± 11.9</td>
<td>19.2 ± 8.4</td>
</tr>
<tr>
<td>Days receiving ventilator</td>
<td>2.8 ± 3.9</td>
<td>5.2 ± 9.1</td>
</tr>
<tr>
<td>Weight at testing, g</td>
<td>1658.9 ± 236.6</td>
<td>1598.8 ± 297.6</td>
</tr>
<tr>
<td>Days consumed FBM</td>
<td>17.5 ± 19.5</td>
<td>11.1 ± 9.8</td>
</tr>
<tr>
<td>Percentage of days consumed FBM</td>
<td>.71 ± .17</td>
<td>.42 ± .32</td>
</tr>
<tr>
<td>Days fed orally prior to testing</td>
<td>17.5 ± 10.5</td>
<td>11.1 ± 9.8</td>
</tr>
<tr>
<td>No. of days visited by mother</td>
<td>18.5 ± 10.0</td>
<td>14.8 ± 8.3</td>
</tr>
<tr>
<td>No. of subjects</td>
<td>14</td>
<td>15</td>
</tr>
</tbody>
</table>

Abbreviation: FBM, fortified breast milk.

*Data are given as mean ± SD unless otherwise indicated.

### Table 2. Mean Number of Sucks and Sucking Bursts During a 10-Minute Observation Period With vs Without Milk Odor Reinforcement in 29 Tube-fed, Premature Infants*

<table>
<thead>
<tr>
<th></th>
<th>With Odor</th>
<th>Without Odor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n = 14)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sucks</td>
<td>290.9 ± 120.8</td>
<td>229.9 ± 157.5</td>
</tr>
<tr>
<td>Bursts</td>
<td>46.4 ± 13.3</td>
<td>35.4 ± 13.0</td>
</tr>
<tr>
<td>Group 2 (n = 15)</td>
<td></td>
<td></td>
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<tr>
<td>Sucks</td>
<td>152.4 ± 160.4</td>
<td>137.3 ± 154.1</td>
</tr>
<tr>
<td>Bursts</td>
<td>27.7 ± 18.1</td>
<td>27.2 ± 16.9</td>
</tr>
</tbody>
</table>

*Data are given as mean ± SD.
to 36 weeks' gestational age, while the mean burst duration for our subjects was 3.1 seconds (data not shown). The relative variability of the individual suck measure compared with the burst measure decreases the utility of this measure for statistical comparisons of NNS activity.

Several lines of evidence underscore the significance of olfactory experience to newborns. Anatomic evidence shows that preterm newborns are endowed with a fully functional olfactory tract. A recent report suggests that associative olfactory learning by human newborns begins in the womb. Newborns' attraction to milk- and maternally derived odors represents a ubiquitous adaptation among mammals. Sullivan et al showed that healthy newborns can form a learned attraction to a novel odor and retain a memory of that odor for 24 hours. These authors also suggested that olfactory associative learning might be adapted to clinical purposes. Together, these findings support the contention that newborns are keenly attuned to olfactory environmental stimuli and that they can learn from their experience with odors.

Pediatrician face conflicting data regarding the effect of pacifiers on newborn feeding. The demonstration of beneficial effects of pacifiers on oral feeding competence in tube-fed premature newborns has led to widespread use of these devices in neonatal intensive care units. On the other hand, concerns that pacifier use may interfere with breastfeeding or promote otitis media in older newborns have led some physicians to discourage their use outside of the neonatal intensive care unit.

We describe a novel method for controlled exposure to nutrient odor during tube feeding. Preliminary results with this technique suggest that nutrient odors may augment oral-tactile stimulation of sucking behavior. These observations provide a basis for further exploration of nutrient odors as therapeutic reagents for tube-fed newborns.

During tube feeding. Conceivably, concerted restoration of nutrient odor to sick newborns may promote oral feeding in this population.

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References