I. INTRODUCTION

In most mammals, a close social relationship exists between a mother and her young which begins at birth and extends to the time of weaning. During this early period the infant comes to recognize the odor of the mother, the species, the nesting area, and the other siblings. In turn, the mother learns to recognize the odor of her infant or infants and, in the extreme case, will not accept offspring for nursing unless the appropriate smell is present. Although recent research suggests that humans also evidence an olfactory infant-mother association, its relative importance for physiological and psychological development is not clear. What is clear, however, is that the human neonate has a functional olfactory system at birth that is responsive not only to maternal odors, but to a wide range of airborne stimulants.

The purpose of this Chapter is to present an overview of the developmental anatomy of the human olfactory system and to discuss what is known about the behavioral responses of neonates to olfactory stimuli, including those present during nursing. The reader is referred elsewhere for more comprehensive and general recent treatises which also present data on the olfactory function of neonates (Doty 1986) and of older children (Mennella and Beauchamp, this book; Moncrieff 1966, Porter 1991, Schall 1988).

II. OLFACUTION IN THE NEONATE

A. Anatomical Considerations

A summary of the prenatal developmental stages of the human olfactory system is presented in Table 1. The human fetus has a well developed ciliated olfactory epithelium
by 9 weeks of age. Completely differentiated olfactory cells are observed by 11 weeks (Pyatkina 1982), while adult-like lamination of the olfactory bulb and a clearly-defined glomerular layer within the extent of the olfactory formation are present by 18.5 weeks (Humphrey 1940). Both periglomerular and interglomerular cells are also observed at this time. By 32 weeks, a modest amount of olfactory marker protein (a probable cytoplasmic enzyme which is unique to olfactory receptor cells) is detectable in the peripheral olfactory nerve layer (Chuah and Zheng 1987).

TABLE 1 : Pre-natal ontogeny of nasal chemoreceptors in humans. Modified from Schall (1988).

<table>
<thead>
<tr>
<th>Gestational Age (post-ovulatory week)</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5 - 5</td>
<td>Formation of the olfactory placode</td>
</tr>
<tr>
<td>4.5 - 6</td>
<td>Formation of the olfactory grooves</td>
</tr>
<tr>
<td>4.5 - 7</td>
<td>Differentiation of the olfactory nerves</td>
</tr>
<tr>
<td>5 - 8</td>
<td>Formation of the vomeronasal grooves</td>
</tr>
<tr>
<td>5.5 - 13</td>
<td>Presence of olfactory-like cells in the vomeronasal regions</td>
</tr>
<tr>
<td>5.8 - 8</td>
<td>Differentiation of terminal-vomeronasal pathways</td>
</tr>
<tr>
<td>6 - 6.5</td>
<td>Formation of the main olfactory bulbs</td>
</tr>
<tr>
<td>6.5</td>
<td>Formation of the accessory olfactory bulbs</td>
</tr>
<tr>
<td>7 - 8</td>
<td>Characteristic structure of the main olfactory bulbs delineated</td>
</tr>
<tr>
<td>7.5 - 9.5</td>
<td>Differentiation of ophthalmic and maxillary divisions of the trigeminal nerve</td>
</tr>
<tr>
<td>9.5</td>
<td>Increase of mitral cell size in the main olfactory bulbs</td>
</tr>
<tr>
<td>11</td>
<td>Presence of ciliated olfactory neuroreceptors suggesting they are ready for reception</td>
</tr>
<tr>
<td>11 18.5</td>
<td>Mitral cell layer clearly delineated in the main olfactory bulbs</td>
</tr>
<tr>
<td>16 24</td>
<td>Presence of epithelial nasal plugs in the external nares</td>
</tr>
<tr>
<td>32 35</td>
<td>Olfactory marker protein present in the olfactory epithelium, olfactory nerve, and bulbar glomerular layer</td>
</tr>
</tbody>
</table>

The trigeminal nerve (cranial nerve V), which mediates intraoral and intranasal somatosensory responses to chemicals (including coolness, warmth, sharpness, and irritation), is well formed in utero (Gasser and Hendrickx 1969, Hogg 1941). Indeed, the
first region of the embryo to be sensitive to cutaneous stimulation (circa 7.5 weeks) is the perioral area supplied by the mandibular and maxillary divisions of this nerve. The ophthalmic division, which innervates the nasal mucosa, is present in month-old embryos and is functional by 10.5 weeks (Brown 1974, Humphrey 1966, Streeter 1908).

Humans possess a well developed vomeronasal organ in utero and, by five weeks of age, olfactory-like sensory cells have been observed in this organ (Bossy 1980, Humphrey 1940, Nakashima et al. 1984, Pyatkina 1982). The lumen of this organ is present in a relatively large number of adults (Johnson et al. 1985) and developed vomeronasal structures have been observed in older fetuses and in the newborn (MacCotter 1915, Read 1908, Kreutzner and Jafek 1980). However, it is unlikely that the vomeronasal system functions postnatally, as the accessory formation, the first relay station of the vomeronasal pathway, undergoes degenerative changes during the second trimester of gestation (Humphrey 1940). Whether the vomeronasal system serves a role in prenatal development or other intrauterine processes is unknown.

B. Neonatal Olfactory Perception

Responses to general odors

A number of researchers in the late 19th Century and early 20th Century reported that odors elicited movements and facial expressions in human newborns, including premature infants as young as seven months (Genzmer 1873, Kroner 1881, Kussmaul 1859, Peterson and Rainey 1910-1911). Although the results indicated that neonates are responsive to odorants, they are inconclusive, since proper controls, such as the use of blank stimuli and blind scoring procedures, were not employed (Disher 1934).

Perhaps the most noteworthy of these studies was that performed by Peterson and Rainey (1910-1911). These investigators tested the behavioral responses of 207 normal term babies, as well as several premature ones, to the odors of asafoetida, oil of rose geranium, compound spirits of orange, tincture of gentian and mother’s milk. Sucking was commonly observed following the presentation of the more pleasant (to adults) odorants (orange extract, oil of geranium), whereas grimaces and head movements were commonly observed following the presentation of the unpleasant odorant asafoetida. In
accordance with more recent work (Sarnat 1978), these authors noted remarkable nasal chemosensitivity in premature infants.

In an effort to overcome the apparent subjectivity of such studies, Engen et al. (1963) used electronic transducers to measure the leg withdrawal, general body activity, respiration and heart rate of 20 neonates (32 to 68 h old) before, during and following the presentation of odorants on cotton swabs. Ten odor trials were alternated with 10 control trials, where non-odorized swabs were presented. In the first of two experiments, significant increases were observed in one or more of the dependent measures after the presentation of either acetic acid or phenethyl alcohol. More responses were observed for the acid than for the alcohol, suggesting that stronger or perhaps more irritating stimulants may be more effective in producing such changes. In the second experiment, anise and asafoetida were presented. Again, both stimuli elicited increases in the responses, with a greater increase occurring for asafoetida, the less pleasant of the two stimuli.

In another series of studies, Lipsitt et al. (1963) sought to explore potential changes in olfactory sensitivity over the first four days of life. They determined an average threshold value each day by presenting successively higher concentrations of asafoetida until a response was elicited. The thresholds decreased as the infants got older, although it is not clear whether this reflected changes in learning, sensitization, olfactory responsiveness, trigeminal responsiveness or motor responsiveness.

Using stimuli they believed to be free from trigeminal activity (anise, asafoetida, valerian and water), Self et al. (1972) evaluated changes in respiration and body movements in 32 newborns before and following odor presentation. Eight subjects were tested daily over three consecutive days, whereas the remainder were tested only once. Although odor-related responses were noted in most of the infants on at least one of the test days, large individual differences were present and a relatively high rate of responding occurred for the water condition. In addition, the same infant rarely gave uniform responses across test days, and the two dependent measures were often in disagreement. Nonetheless, odor-related responses were observed in both irregular and deep sleep, and subjects tended to consistently fall into low, moderate, or high levels of responding.
Following in the tradition of a number of early studies which noted that odors elicited facial responses in newborns (Ciurlo 1934, Peterson and Rainey 1910-1911, Stirnimann 1936), Steiner (1974, 1977, 1979) found that odorants such as banana extract, vanilla extract and butter produced smile-like expressions accompanied by sucking movements in neonates less than 12 h old, whereas shrimp and rotten egg odors elicited rejection-like responses, such as a depression of the mouth angles and lip pursing. Steiner recorded such responses cinemagraphically and observed that they also occurred in anencephalic infants.

Overall, these studies imply that neonates respond to odorants. However, since many of the stimuli used in a number of these studies likely had considerable trigeminal stimulative properties (Doty et al. 1978), some of these findings may reflect stimulation of the latter nerve rather than stimulation of the olfactory system. Evidence in support of the hypothesis that many of the behavioral responses are due to olfactory, rather than trigeminal stimulants, should include the demonstration of 1) clear-cut responsiveness to relatively non-irritating stimuli, and 2) differential responsiveness to qualitative, rather than intensive, aspects of the stimuli. Assuming that infants have a trigeminal system of similar sensitivity to that of the adult, the reliable elicitation of sucking and other behaviors in the neonate by odorants such as butter, vanilla, phenethyl alcohol and anise would appear to be in accord with point (1). The differential responding noted to several other types of stimulants, along with more recent studies (described in detail below), which demonstrate that newborn infants can distinguish their own mothers' breast and axillary odors from those of other mothers, provide examples of point (2).

C. Responses to Odors in the Maternal Environment

In two simple but elegant pioneering studies, Macfarlane (1975) demonstrated that neonates could distinguish the odor of their own mother's breasts from 1) a blank control and 2) that of other lactating females. In the first study, Macfarlane hung, side by side, a clean breast pad and a breast pad worn previously by its lactating mother in a test crib where a neonate was lying supine. The pads just touched the baby's cheeks. Videotape records revealed that 17 of the 20 subjects, who were between 2 and 7 days of age, spent more time orienting towards the mother's breast pad than towards the clean breast pad.
The majority of the time spent orienting towards either pad was directed towards the mother's pad.

In the second study 32 neonates were similarly tested on days 2 and 6 post-partum for their reactions to breast pads previously worn by their mothers vs pads previously worn by a strange lactating mother. A separate group of 32 infants within the age range of 8 to 10 days was also tested. The percentage of time spent turned towards one or the other
breast pad was 72.3 on day 2, 82.6 on day 6, and 89.4 on days 8-10. The percentage of time spent oriented towards the breast pad of their own mother, as a percentage of the total time spent with both breast pads, of the three age groups was 51.8, 60.3 and 68.2% respectively. Fifty-three percent of the babies turned more towards their own mother’s pad at 2 days of age (not significantly different from chance), whereas 69% and 78% did so at 6 and 8-10 days of age, respectively (respective ps < 0.01 and 0.001).

In a less structured test situation, Russell (1976) presented breast-fed neonates with 1) a clean moist breast pad, 2) a pad previously worn by the infant’s mother, and 3) a pad previously worn by another lactating mother. Although reliable differences in responding were not observed at 2 days of age, by 2 weeks of age 8 of the 10 infants responded to the odor of their own mother and 7 of the 10 to that of the strange mother. Three responded solely to the odor of their own mother. By 6 weeks of age, 6 babies responded only to their own mother’s odor and one responded to both the odor of its own mother and to that of the unfamiliar mother.

Using a test paradigm similar to that devised by Macfarlane (1975), Cernoch and Porter (1985) demonstrated that preferences for maternal odors are not confined solely to stimuli from breast pads of the mother. Thus, two-week old breast-fed neonates preferentially oriented towards axillary odors from their mother relative to axillary odors from 1) another lactating mother, or 2) a non-lactating unfamiliar mother. Since bottle-fed infants failed to show this phenomenon, it would appear that either breast and axillary odors have elements in common, or the act of breast feeding brought the infants into closer proximity to the axillary stimuli. No preference was observed when the axillary odors of the father were compared to those of an unfamiliar male.

Support for the role of learning in producing such preferences comes from a study by Schleidt and Genzel (1990). Lactating women applied perfume to their breasts, but not to their nipples, before their babies nursed. When tested at 1 and 2 weeks of age, the infants oriented more towards the familiar perfume than towards a novel one. At 4 weeks of age (2 weeks after the mothers stopped perfuming their breasts), most of the infants failed to demonstrate a preference for the originally-presented odorant, suggesting that the preference may extinguish without repeated presentation or conditioning.
Balogh and Porter (1986) found that exposure to odors without any known conditioned reinforcers is sufficient to induce at least some types of odor preferences in neonates. These investigators taped pads odorized with either ginger or cherry inside the bassinets of babies less than 22 h after birth. On the following day, female neonates oriented more towards a pad impregnated with the exposure odor than with a control odor. The males evidenced no such preference and exhibited a bias in turning their heads to the right regardless of the position of the stimulants. The authors suggest that this difference in the behavior of the sexes may be a reflection of the sex difference in the performance of a number of olfactory tasks that is well-documented in older infants and in adults (Doty et al. 1984, 1985, Deems and Doty 1987, Koelega and Koster 1974, Wallace 1977).

The results of the above studies, along with observations that maternal odors can quiet restless babies (Schall et al. 1980), provide strong evidence that newborn infants have a keen sense of smell. Whether there is any meaningful post-natal development in the perception of the quality of odors is unknown, although there is evidence that sensitivity to odors may be enhanced in adulthood by repeated psychophysical testing or odor exposure (see Chapter 5, this book).

D. Responses to Irritating Vapors

Currently there appears to be only one study that has systematically examined the responsiveness of neonates to irritating odors (Rieser et al. 1976), concluding that newborns are capable of responding directionally to the presence of irritating vapors. These investigators videotaped movements of infants ranging in age from 16 to 131 h following the brief presentation of two open-ended glass sleeves in front of their nares, one containing a low concentration of ammonium hydroxide and the other no odor. On 64% of 304 trials the newborns turned away from the side with ammonia, and on 30% they turned towards that side. As in studies of responsiveness to touch and sound (Turkewitz et al. 1966), the infants exhibited a bias in turning to the right, conceivably reflecting neonatal cerebral asymmetries (Wada et al. 1975).
III. SUMMARY AND CONCLUSIONS

Six general conclusions can be made from the studies reviewed in this Chapter: 1) The human olfactory system is functional at birth; 2) human neonates exhibit facial responses resembling those of pleasure following the presentation of odorants which are judged by most adults as pleasant and of displeasure following stimulation with odorants perceived by adults as unpleasant; 3) human neonates can detect, by inhalation, air-borne irritants such as ammonia, and can localize the direction from which they are presented; 4) newborn babies learn to distinguish between, and come to prefer, odors of their own mothers to those of other lactating mothers; 5) maternal odors can decrease the movements of a baby, and 6) exposure to odorants without traditionally paired reinforcers can influence odor preferences early in life. The degree to which long-lasting odor preferences can be induced, however, is unknown and may well depend upon the age of the infant and the nature of the stimulus presented.

REFERENCES

Ciurlo, L (1934) Sulla funzione olfattoria nel neonato. Valsalva 10: 22-34
Disher DR (1934) The reactions of newborn infants to chemical stimuli administered nasally. In: Dockeray FC (ed) Studies of infant behavior. Ohio State University Press, Columbus, p 1
Gasser RF, Hendrickx AG (1969) The development of the trigeminal nerve in baboon embryos (Papio sp.). J Comp Neurol 136: 159-182
Genzmer A (1873) Untersuchungen ueber die Sinneswahrnehmungen des neugeborenen Menschen. Inaugural Dissertation, Halle
Hogg ID (1941) Sensory nerves and associated structures in the skin of human fetuses of 8 to 14 weeks of menstrual age correlated with functional capability. J Comp Neurol 75: 371-410
Humphrey T (1940) The development of the olfactory and the accessory olfactory formations in human embryos and fetuses. J Comp Neurol 73: 431-468
Kussmaul A (1859) Untersuchungen über das Seelenleben des neugeborenen Menschen. C.F. Winter'sche Verlagsbuchhandlung, Leipzig und Heidelberg
Stirnimann F (1936) Versuche uber Geschmack und Geruch am ersten Lebenstag. Jhb Kinderhik 146: 211-227