Breast-feeding and the Mother

Ciba Foundation Symposium 45 (new series)
Breast-feeding and the Mother
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Chairman's introduction

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The decline in breast-feeding in many societies has become a subject of major concern to health workers throughout the world. It is not surprising then that breast-feeding has already been discussed in two recent symposia held at the Ciba Foundation—on parent–infant interaction in November 1974 and on diarrhoea in childhood in October 1975 (Ciba Foundation 1975, 1976). Some of the members of this symposium participated in those meetings but others did not and none will yet have read the report of the second meeting because it is being published in July 1976. I shall therefore review briefly the major points made at these meetings in relation to breast-feeding in order to form a basis for our discussions.

In the symposium on Parent–Infant Interaction, Dr J.F. Dunn (1975) reminded us that success in breast-feeding appeared to be correlated more with prenatal enthusiasm, the educational level of the mother, and the support she receives than with the ease or difficulty with which breast-feeding is established during the first days after birth. Nevertheless, Dr J.H. Kennell presented evidence that mothers who suckled their infants immediately after birth—that is, while still on the delivery table—were much more likely to be breast-feeding two months after the birth than mothers who did not begin to feed their infants until later. Dr R. Sosa elaborates on this aspect elsewhere in this volume (pp. 179–188).

Drs P. Johnson and D.M. Salisbury described studies on breathing and sucking and showed that, whereas all bottle-fed babies tended to behave in a similar manner during feeding—with sucking being continuous and breathing irregular—the behaviour of babies who were breast-fed varied considerably but, in general, their sucking was episodic and their breathing was more regular. The question was asked as to whether it was the baby, the milk or the type of feeding that caused the difference. The evidence that was presented suggested
that it was the type of fluid (i.e. the milk) rather than the reservoir (i.e. the breast or bottle) that modified the pattern of behaviour. Dr J. A. Macfarlane emphasized the importance of smell; babies were shown to turn towards their mothers' breast-pads rather than to clean pads or the pads of other mothers. Although it seems likely that the specific smell comes from the skin of the mother rather than from her milk, the contribution of the smell of milk has not been fully established.

Dr Dunn also discussed the relation of the behaviour of both mother and baby to the type of feeding. Mothers who were breast-feeding tended to touch, rock and smile at their babies more often than those who were bottle-feeding. The end of a bout of feeding was almost wholly controlled by the mother of the bottle-fed baby but with breast-feeders either mother or baby could control it. No obvious difference could be detected in the interaction patterns of the breast-fed and bottle-fed babies later in infancy but it was felt that this might be due to the fact that the level of analysis was not fine enough. The importance of synchrony between mother and infant was highlighted by Dr J.S. Rosenblatt who described how the nipples of lactating rats were altered to respond to the sucking patterns of the pups at different ages.

The final point I would draw out of that symposium is the important concept of the social meaning of breast-feeding and of bottle-feeding to the mother, a concept which was brought up in discussion by Dr M.P.M. Richards and which we should surely take up again in our discussions.

In the symposium on Acute Diarrhoea in Childhood, the role of infant-feeding practices in pathogenesis generated considerable discussion. Amongst the merits of breast-feeding in protection against gastroenteritis, the immunological aspects were given a great deal of attention and Dr N.F. Pierce speculated on the mechanism by which the breast 'learnt' to produce IgA antibodies to enteric antigens. It was also stressed that much more work was needed before claims could be made about the effects of antibodies and of lactoferrin in bacterial infections other than those caused by E.coli. The question of the sterility of breast milk and the problems associated with hyperelectrolytaemia were also discussed and Dr D.A.J. Tyrrell presented some preliminary observations about an inhibitory substance to viruses present in breast milk.

As may be imagined, the discussion on breast-feeding ranged much wider than the topic of gastroenteritis and included other medical aspects such as hypocalcaemia, sudden infant death, obesity, and atherosclerosis and also social aspects such as the provision of crèches for mothers at work.

After this brief survey of breast-feeding arising out of two symposia whose main subjects were not breast-feeding, we may well ask what new material can be contributed in this symposium whose main subject is breast-feeding. May I
then remind you that in nearly all the papers I have mentioned the emphasis has been on the baby; the effect of breast-feeding on the infant has been the prime object of study. But breast-feeding is a process based on partnership. The effects on the mother, who should be an equal partner with her baby, should be of equal concern. Possibly we should be even more concerned for the mother because, whereas for a baby who cannot be breast-fed there is a substitute food, however imperfect, for the mother who cannot breast-feed there is no real substitute. Dr Katherine Elliott, sensing that concern for mother and baby has swung rather far towards the baby, has sought to restore the balance through this symposium. Our function is primarily to consider the mother and my instructions from Dr Elliott were 'to dispose of the baby'. I hope that I have reassured you that we can safely do this because much attention has been already given to the baby. Therefore, in all our discussions I want us to keep the mother in the forefront of our attention although, of course, I do not expect that we shall totally neglect the infant.

Our programme starts with physiology, moves to psychology and culture, and finishes with strategy and politics. This mixture is surely guaranteed to deepen our understanding and stimulate our discussions. By the end of the symposium, I hope we shall have contributed to a more balanced approach to breast-feeding.

References

Pituitary-adrenal responsiveness of rat mothers to noxious stimuli and stimuli produced by pups

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Abstract  Studies on the response of female rats to various stresses during the course of lactation showed a marked reduction in pituitary-adrenal activity. Maximum suppression coincided with the period of maximum lactation, about 14 days after parturition. Both pituitary corticotropin and the release of corticosterone were significantly reduced. Females showing maternal behaviour but not lactating did not exhibit this buffering of the stress response.

Another aspect of pituitary-adrenal activity has been studied in lactating female rats. Females, although they have a buffered stress response, responded differently, in terms of pituitary-adrenal activity, to stimuli emitted by the pups: pups which are exposed to noxious stimuli elicit a much greater pituitary-adrenal response in lactating females than do pups which are merely handled. Separation from the pups does not elicit a pituitary-adrenal response. This difference in response is modified if the infants are malnourished and is not observed in virgin animals that are not lactating.

PITUITARY-ADRENAL ACTIVITY DURING LACTATION

There has been extensive research on the mechanisms controlling lactation and maternal behaviour. Maintenance of the offspring dramatically changes the behaviour and physiological states of the rat. However, in recent years it has become apparent that other striking physiological and behavioural changes accompany lactation.

We shall review two major changes in the psychobiology of the lactating rat: changes in the lactating female's diurnal rhythms and responsiveness to stress as measured by pituitary-adrenal activity and changes in the mother's response to various stimuli emitted by her pups, also reflected by alterations in pituitary-adrenal function.

Several years ago, we examined the response of lactating animals to pentobarbital anaesthesia. We found that the temperature did not fall in lactating
rats after anaesthesia as it did in virgin females (Thoman et al. 1968) and also that the marked rise in the plasma concentration of corticosterone in non-lactating females after anaesthesia was much less in the lactating rats. Furthermore, lactation diminished the rise in the plasma concentration of corticosterone that accompanied either fighting induced by shock or exposure to ether (Thoman et al. 1970a). These results led to the development of the hypothesis that the lactating female is buffered against disturbing stimuli.

To put our studies on adrenocortical responsiveness to noxious stimuli in lactating rats into perspective, we must review the role of the pituitary-adrenal system during lactation. Glucocorticoids are important in the initiation and maintenance of lactation in the rat and in other species (Cowie & Tindal 1971). Rats whose adrenals have been removed will lactate although not as well as normal animals (Cowie & Folley 1947; Thoman et al. 1970b) but when glucocorticoids are injected the lactational deficiency resulting from adrenalectomy is reversed (Cowie & Folley 1947), by direct action on the mammary gland, as shown in cultures in vitro (Elias & Rivera 1959), and on biochemical pathways in the mammary gland (Greenbaum & Darby 1964; Willmer & Foster 1965). Injection of ACTH (corticotropin) into lactating ruminants generally depresses the secretion of milk (Brush 1960; Flux et al. 1954) but appropriate doses of cortisol acetate, hydrocortisone acetate and corticosterone enhance lactation in rats (Hahn & Turner 1966; Johnson & Meites 1958; Talwalker et al. 1960). Thatcher & Tucker (1970) suggested that, late in lactation, the decreased adrenal secretions become rate-limiting for milk production in rats.

Suckling powerfully stimulates the release of prolactin and oxytocin (Meites 1966), the hormones necessary for the secretion and release of milk. It also stimulates the discharge of corticotropin in goats, sheep (Denamur et al. 1965) and rats (Grégoire 1947/48; Voogt et al. 1969) (see Cowie & Tindal 1971 for a more extensive discussion of the suckling stimulus and its neuroendocrinal consequences). Although it is adaptive for suckling to induce the release of corticotropin, which enhances milk secretion, we are faced with the question of whether suckling is in some way stressful, since release of corticotropin is usually associated with stressful stimuli. Presumably breast-feeding, which postpartum animals do spontaneously and repeatedly, is not a noxious experience. However, the tactile stimulus to the teat must be intense and arousing since it elicits the release of oxytocin (Tindal & Knaggs 1970). The metabolic demands of lactation might be thought of as a stressor.

Generally, the plasma concentration of corticosterone increases in the morning as a consequence of suckling (Kamoun 1970a,b; Voogt et al. 1969). This fact appears to be consistent with previous indices of adrenal hyperfunction during lactation, such as adrenal hypertrophy, adrenal depletion of ascorbic acid and
adrenal increases of cholesterol. If the adrenal glands are hyperactive during lactation, it seems paradoxical that the pituitary–adrenal response to environmental stressors is reduced at this time. This reduction is found with not only potent physiological stressors, such as pentobarbital, shock and ether, but also relatively mild stimuli, such as that which a rat may experience on being placed in a novel arena (an open field) for three minutes.

To understand further the dynamics of the pituitary–adrenal activity of the lactating rat, we measured basal and stress secretions of plasma corticosterone over 24 h. We also measured the effects of ether on the plasma concentrations of corticotropin in suckling rats and the changes in adrenal and plasma concentrations of corticosterone when we injected the rats with corticotropin (Stern et al. 1973). In all these experiments female Sprague–Dawley rats were individually housed with their litters and maintained on a schedule of 12 h of light daily. We measured the plasma corticosterone concentration by a microfluorometric method (Glick et al. 1964) and plasma corticotropin by a mouse bioassay (modified from that of Hedner & Rerup 1962).

The non-lactating, postparturient rat shows the typical diurnal rhythm of plasma corticosterone of a rat with a six-fold difference between low (early morning) values and late afternoon–early evening peaks (Fig. 1). High concentrations in the lactating rats in the morning almost obliterated the circadian

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**Fig. 1.** Circadian variation in plasma concentrations of corticosterone in lactating (○) and non-lactating (●) rats in basal and stress (ether) conditions. Each point (and vertical bar) is the mean (±S.E.M.) of eight rats. (Taken from *Neuroendocrinology* 12, [1973], by permission of S. Karger AG.)
TABLE 1

<table>
<thead>
<tr>
<th>Condition</th>
<th>Plasma corticosterone (µg/100 ml)</th>
<th>Plasma corticotropin (mU/100 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n base stress</td>
<td>n stress</td>
</tr>
<tr>
<td>Non-lactating</td>
<td>8 5.0±0.4 76.9±4.8</td>
<td>6p 6.6</td>
</tr>
<tr>
<td>Lactating (continually)</td>
<td>6f 16.7±1.9d 44.2±1.9d</td>
<td>5c 2.2f</td>
</tr>
<tr>
<td>Non-lactating</td>
<td>4 6.6±1.1 65.5±7.1</td>
<td>4 9.1</td>
</tr>
<tr>
<td>Lactating (litter-deprived)</td>
<td>4 11.7±3.9 39.0±2.2e</td>
<td>4 3.3f</td>
</tr>
</tbody>
</table>

Values are quoted as mean ± S.E.M.

Four samples from individual rats plus two samples of plasma pooled from two rats each.

This group originally consisted of eight animals: one died before any blood samples could be obtained and the basal sample of another animal was lost. Plasma from the latter rat plus that of two others was combined to form one pool for corticotropin analysis. The other four corticotropin samples were from the remaining four females in this group.

P<0.001 compared to non-lactating controls.

P<0.01 compared to non-lactating controls.

P<0.05 compared to non-lactating controls.

This increase is probably due to release of corticosterone induced by suckling because we have found that the morning basal concentrations of plasma corticosterone in female rats deprived of their litters for 24 h did not differ significantly from those in non-lactating controls. Fig. 1 also shows that 15 min after exposure to ether and jugular venepuncture, the pituitary–adrenal activity of lactating rats is less than that of postparturient non-lactating control animals. This reduction can be observed throughout the 24 h cycle. The acute time-course of the changes in plasma corticosterone concentrations after exposure of the rat to ether showed that the reduced stress response is not an artifact of the 15 min sampling procedure (Zarrow et al. 1972). In another study we found that the concentrations of plasma corticotropin in stressed rats were about one-third of the values in non-lactating controls (Table 1). Thus the reduced response to stress is not due to some change in adrenal metabolism but is related to some central process which regulates corticotropin. Kamoun (1970b) suggested that the pituitary–adrenal secretions after stress during lactation are reduced as a result of feedback inhibition by suckling-induced rises in plasma corticoid concentrations. This explanation is not wholly satisfactory in view of the lowered plasma corticotropin and corticosterone concentrations in both continuously lactating and 24 h deprived lactating rats, a difference which indicates that recent suckling experiences and their consequences are not essential for the diminished pituitary–adrenal responsiveness to stress.

The reduced rise in plasma corticotropin concentrations in lactating rats in
response to ether indicates that a pituitary or central nervous system component is partially responsible for the reduction in plasma corticosterone concentrations after stress. But we have evidence that a peripheral component may also lower the plasma concentrations of corticosterone in stress (Stern et al. 1973). Secretion of corticotropin can be blocked in rats by pretreatment of the rats with a potent synthetic glucocorticoid, dexamethasone. Injection of corticotropin into lactating rats treated with dexamethasone resulted in higher adrenal and lower plasma concentrations of corticosterone.

Finally, we asked whether lactation was necessary for this altered pituitary-adrenal activity or whether maternal activity in the postpartum rat, with no suckling stimulation, could bring about this change. A mother rat whose nipples were removed ('thelectomy') before conception behaves normally when she is confronted with pups that have been nursed by donor females (Moltz et al. 1967). Endocrine changes similar to those in lactation are induced by this procedure (Moltz et al. 1969), but the interaction between mother and pup in the absence of suckling was not sufficient to diminish the rises in corticotropin and corticosterone concentrations after ether stress (Stern & Levine 1972). Clearly, physiological changes in the suckled rat but not in the thelectomized or litter-deprived postpartum rat must account for the differences in pituitary-adrenal responsiveness.

Whether the lowered corticosterone concentrations and reduced responsiveness to stress are functionally significant remains to be clarified. High plasma concentrations of corticosterone in the mother might mean that corticosterone can reach the pup through the milk and so deleteriously affect the development of the young (Schapiro 1968). However, as only trace amounts of corticoids seem to pass from mother to pup through the milk, this postulate appears to be negated (Zarrow et al. 1970). Postnatal maternal stress alters the pituitary-adrenal response and behaviour of the offspring (Levine & Thoman 1969; Thoman & Levine 1969). Thus pituitary-adrenal secretions, reduced by stress, may modify behaviour per se or they may reflect modifications by stress of other behavioural and physiological changes. The mother's behaviour toward her litter is possibly more stable when her responsiveness to stress is reduced, as she would be less disturbed by changes in her environment.

In all these studies on pituitary-adrenal responsiveness in the lactating female rat, we have used traditional methods of activating the pituitary-adrenal system, such as ether, shock, or exposure to a novel environment. Although the response to these stimuli is buffered, the evidence we shall now present indicates that the mother can be selective in her response to stimuli produced by pups and responds in certain specific conditions to the treatments imposed on the pups.
MATERNAL PITUITARY-ADRENAL RESPONSIVENESS TO OFFSPRING: DIFFERENTIAL CHANGES ELICITED BY TREATMENTS TO THE PUPS

Research into the interactions between mother and infant in both humans (Bell 1971; Harper 1975) and rats (reviewed by Russell 1971) has emphasized that these interactions are dyadic and reciprocal; that is, offspring are not passive recipients of maternal stimulation (Ressler 1962, 1963) but provide cues that initiate (Herrenkohl & Lisk 1973), direct (Smotherman et al. 1974) and coordinate maternal behaviour (Harper 1971).

Although others have reported that early experiential treatments to rat offspring produce lasting behavioural and physiological changes (Denenberg & Zarrow 1971; Levine 1962), the mechanisms by which these treatments exert their effects are not clear (for reviews, see Daly 1973 and Russell 1971). Some workers have suggested that the effects of early experience are due in part to the changes in the mother's behaviour (Bell et al. 1971; Thoman & Levine 1970) when the pups are returned to her after the manipulations. Bell et al. (1974) have suggested that in some instances changed patterns of maternal behaviour prolong the stress of the separation and of the early experience treatment. Furthermore, the rat mother is sensitive to the behaviour or quality of stimulus (or both) of her progeny (Meier & Schutzman 1968; Young 1965) and systematic changes in her behaviour depend on the nature of treatment (e.g., intensity) her offspring have received (Barnett & Burn 1967; Bell et al. 1974).

Specific stimuli associated with pups trigger corticotropin/corticosterone changes in females exposed to the stimuli. Voogt et al. (1969) found that rat pups kept near their mother but not allowed to suckle stimulated the mother's adrenal secretion of corticosterone. In another study, rat pups presented to lactating females either directly or indirectly (i.e. behind a wire mesh screen) elicited a corticosterone response (i.e. secretion). This pattern of corticosterone change in the lactating female differed from (i.e. was more sustained than) that shown by the virgin female (Zarrow et al. 1972).

In view of these findings we initiated the present series of experiments to examine maternal pituitary-adrenal responsiveness, focusing on the mother's physiological, rather than behavioural, responsiveness to pups. We exposed mothers to litters of pups that had received different treatments (i.e. handling or shock) while out of the nest. The mother's blood was sampled 20 min after reunion and the changes in plasma concentrations of corticosterone as a result of the stimuli of the pups' presence were determined. We chose the pituitary-adrenal system as an index of maternal responsiveness because this system is a sensitive measure of an animal's response to changes in its environment (Friedman et al. 1967; Levine 1962).

In all the studies we report in this paper, we followed a similar procedure of
separation—manipulation—reunion. After a mother had been separated from her litter she was kept in a holding cage while we manipulated the litter. The pups in the litter were either shocked (0.4 mA for 90 s) or handled (removed from home cage by the experimenter). After the treatment, the mother and her litter were reunited in the home cage. In all the experiments, the litters were returned enclosed in wire mesh baskets so that the mother could not make direct contact with the pups while she was exposed to the stimuli from her pups.

In our initial experiment and a second replication in the same conditions, we took samples of blood from groups of mothers reunited with litters in which the pups had been shocked or handled. The concentrations of corticosterone in these mothers were compared with those in mothers sampled while they interacted with undisturbed litters (basal samples). We designed this latter sampling procedure to enable us to determine the resting concentrations of corticosterone in plasma. Mothers reunited with handled or shocked litters showed increases in plasma corticosterone (Fig. 2). More importantly, however, with the same conditions of separation and reunion, plasma concentrations of corticosterone were higher in mothers reunited with shocked pups than in mothers reunited with handled pups (Smotherman et al. 1976). This pituitary-adrenal responsive-
Mothers' plasma corticosterone concentrations in response to separation from her pups. Data are plotted separately for litter removal group (R) and disturbance control group (C). Mothers were sampled after treatment on days 7 and 14 of lactation (n=8 mothers for each data point).

Fig. 3. Mothers' plasma corticosterone concentrations in response to separation from her pups. Data are plotted separately for litter removal group (R) and disturbance control group (C). Mothers were sampled after treatment on days 7 and 14 of lactation (n=8 mothers for each data point).

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ness of the mother on reunion with her pups confirmed the findings of Zarrow et al. (1972). Furthermore, mothers showed different responsiveness depending on the intensity of treatment their pups received during the separation period.

Although this initial experiment and its replication demonstrated that shocked pups elicited a greater corticoid response than handled pups, it did not allow us to decide whether the increases in corticosterone concentrations in the mothers reunited with handled pups resulted from the mothers’ response to pups or whether they were a more generalized response to the disturbances associated with the procedure of separation, treatment and reunion (e.g., cage movement, handling, placement of the wire mesh baskets). Therefore, we determined the changes in corticosterone concentration in the lactating female when her litter was removed and, further, her corticoid responsiveness specific to the treatment of the pups.

Fig. 3 shows plasma corticosterone concentrations for groups of lactating females at various times after separation from their litters. We compared the mothers in the litter-removal groups with the mothers in the disturbance-control groups that received treatment identical to that of mothers in litter-removal groups (i.e., handling, brief separation from the litter, return to their home cage) but whose litters were not removed or disturbed. We determined corticosterone
concentrations after these treatments on day 7 and again on day 14 of lactation. We found that maternal corticoid concentrations were higher than basal values (at both 30 and 60 min) in both groups. Separation was, however, without an effect as the pattern of elevations was the same for both groups. Litter removal per se did not activate the mother’s pituitary–adrenal system more than handling her did.

To assess maternal responsiveness to pups at a time after separation when maternal corticoid concentrations had returned to basal levels (i.e., when they had recovered in terms of pituitary–adrenal activity from the initial stress of the separation procedures), we removed the pups, treated them and returned them after a three hour period of separation. In this way any changes in response to pups would be imposed on resting concentrations rather than on concentrations already raised by the removal of the litter. We hoped that this procedure would provide a more sensitive measure of the mother rat’s corticoid response to stimuli her pups produced. In addition, Zarrow et al. (1972), using a similar method, found that after a three-hour separation the mothers’ corticoid concentrations had returned to resting values.

Mothers were reunited with litters (in baskets) that had been handled or shocked just before the end of the separation period. Samples of blood were taken from the mothers 20 min after reunion. We sampled additional groups of mothers (also separated from pups for three hours) to determine post-separation basal values or we exposed them to an empty wire-mesh basket to determine the change in corticosterone concentrations in response to the novelty of the basket. These separation–treatment–reunion procedures were followed and mothers’ blood was sampled on days 7 and 14 of lactation (Fig. 4).

Mothers reunited with handled or shocked litters had higher plasma concentrations of corticosterone than those of mothers in the basket-control group. Mothers reunited with shocked pups again showed rises that were significantly higher than those of mothers reunited with handled pups. This pattern of responsiveness was the same as that found after brief separation, treatment of pups and reunion. Fig. 4 also shows that there is an effect due to the stage of lactation. Although the overall pattern of responsiveness was the same on both day 7 and day 14 of lactation, the magnitude of the response was less on day 14. This overall diminished pituitary–adrenal responsiveness later in lactation has been previously observed (Stern & Levine 1974).

To summarize, we have found that maternal corticoid concentrations did not increase in response to litter separation. In the experiments where mother and pups were reunited after separation, a differential pattern of maternal corticoid responsiveness emerged: mothers reunited with shocked pups showed pituitary–adrenal activity significantly greater than that of mothers whose pups had been
handled before reunion. Different treatment of the pups during separation apparently changed their stimulus qualities to which the mothers responded with different pituitary–adrenal activation. Even though the data reveal nothing about the cues involved, the results were not due to changes in interactions between mother and infant since, after the handling or shock, pups were placed in a wire-mesh basket and in this way direct mother–infant interaction was prohibited.

In the absence of direct interactions it is likely that changes in maternal corticoid concentrations are elicited by exteroceptive stimuli (e.g., auditory, olfactory, visual) produced by the pups. Treatments to pups such as those we used (e.g., handling or shock) stimulate pups to produce ultrasonic sounds (Bell et al. 1971; Noirot 1972; Okon 1971). Bell (1974) has suggested that these neonatal sounds arouse the mothers exposed to them. In support of this hypothesis, Smotherman et al. (1974) found that ultrasounds served as directional cues and combined with pup-associated odours to guide the lactating female’s retrieval response. Although we did not measure the pup vocalizations in these experiments, increased rates of ultrasonic vocalizations as a result of the
shocking procedure may constitute the effective stimulus, thereby eliciting a more vigorous pituitary–adrenal response in the lactating female exposed to shocked pups.

The role of olfaction in affecting maternal corticoid responsiveness cannot be discounted. Pup odours affect the release of corticosterone (Zarrow et al. 1972). In mothers reunited with pups after a three hour separation period, the lactating female’s corticoid response to her pups depended on olfactory stimulation since females that had received bilateral olfactory bulbectomy failed to show the rises in corticoid concentrations induced by pups.

Whatever the cues, there is considerable evidence for varied behaviour of the rat mother in response to her pups. Rat mothers can be sensitized by exposure to exteroceptive cues from pups (Herrenkohl & Lisk 1973). Reisbick et al. (1975) have reported that not only are stimuli associated with pups important for the maintenance of maternal behaviour but that the decline in maternal responsiveness may be synchronized by stimuli from the pups. Others have reported that treatment of the pups which changes their qualities in ways that are discernible to their mothers leads to changed patterns of maternal behaviour when mother and infant are reunited (Bell et al. 1971; Meier & Schutzman 1968; Young 1965). Bell et al. (1974) have further demonstrated that the intensity of treatment given to pups is reflected in changed patterns of maternal behaviour. Our studies on maternal pituitary–adrenal responsiveness complement these behavioural data.

Rosenblatt (1969) has demonstrated that patterns of maternal behaviour change during the preweaning period: an initial phase of intense maternal behaviour (i.e., during the first postpartum week), initiated primarily by the mother and cued by stimuli from the pups (Smotherman et al. 1974), is followed in the third postpartum week by a period during which the pup initiates contact with the mother; the contact is controlled by stimuli emanating from the mother (Moltz & Leon 1973). Furthermore, there exist ontogenetic changes in the cues (e.g., ultrasonic vocalizations) provided by the infant rat (Noirot 1972; Okon 1971). These cues, as stated above, coordinate sequences of maternal behaviour. In addition, the pituitary–adrenal responsiveness of the lactating female to stressors (Stern & Levine 1974) varies as a function of the stage of her lactation.

For these reasons we examined the ontogeny of the mother rat’s differential pituitary–adrenal responsiveness to her pups. Again the separation–manipulation–reunion procedure was used with individual groups of mothers being exposed to their pups after the pups had been handled or shocked. Mothers were tested with their litters twice during lactation, the second treatment nine days after the first. Thus, each mother was tested on postpartum days 2 and 11, 5 and 14, or 8 and 17 (Fig. 5). We found ontogenetic changes in the corticosterone response. Mothers showed equally high corticoid concentrations in
response to shocked pups throughout lactation. However, on days 2 and 5 of lactation, the amount of corticosterone in response to handled pups was as great as the amount evidenced by females in response to shocked pups. Not until day 8 of lactation did we see the differential responsiveness to handled and shocked pups that we observed in previous experiments. Early in lactation (during the first five postpartum days), mothers showed a maximal corticoid response to pups independent of which treatment the pups had undergone. These data parallel closely the behavioural data (e.g., the initial stage of the intense maternal responsiveness during the first week after parturition) reported by Rosenblatt (1969).

Other investigators have also indicated that newborn pups can restore maternal behaviour in mothers who no longer exhibit such behaviour towards their own litters (Rosenblatt 1969; Thoman & Levine 1970). These findings suggest that the age of the pups as well as the stage of lactation is potentially an important variable affecting maternal corticoid responsiveness. We are currently testing mothers at different stages of lactation with pups of different ages to assess whether these ontogenetic changes in responsiveness are mediated by the stimuli produced by the pups, the mother's stage of lactation or an interaction of these two factors.

So far, we have used the term maternal responsiveness to mean that the changes in corticoid concentrations we observed were peculiar to, and would be shown only by, lactating females. Since several studies (Fleming & Rosenblatt 1974; Rosenblatt 1975) have shown that virgin females can show maternal
behaviour in response to pups, we presented virgin females and males with fostered test pups of three ages—2, 9 or 16 days—that had been handled or shocked and determined their plasma corticosterone concentrations (Fig. 6). Each virgin and male was repeatedly tested with the same litter at each of these ages. Virgins and males were housed in a room separate from the donor mothers and litters so that the only time the test animal was exposed to pups was during the test periods—about 20 min on each of three occasions. Baskets were placed in the cages of both males and virgins three days before testing and were left there for the duration of the experiment. On the day of testing, the animal (male or virgin female) was removed briefly from its cage for two minutes and its basket was replaced with a basket containing either shocked or handled pups. In the basket control experiment, we simply removed the test animal for the two-minute period. The results indicated that the characteristic differential responsiveness shown by the lactating female was not shown by either virgin female rats or male rats regardless of the age of the stimulus pups. At no point did responses to either handled or shocked pups differ from responses to the empty basket. These results together with results from experiments with lactating females strongly indicate that the pattern of differential corticosterone responsiveness observed is peculiar to lactation.

![Graph](image)

**Fig. 6.** Corticosterone responsiveness of male and virgin female rats to pups aged 2, 9, or 16 days that had been handled (H) or shocked (S). Responses of animals presented with an empty basket (BC) are also shown. Entries represent mean values (n=8 subjects/bar). Vertical lines above bars represent the standard error of the mean.

**CONCLUSIONS**

The data presented in this paper represent an interesting and perhaps important aspect of lactation. Initially we observed that the lactating rat had what
we have called a buffered response to environmental change (stress). Thus, in a variety of conditions, lactating females invariably demonstrate a marked and significant reduction in the pituitary–adrenal activity that is normal in non-lactating animals experiencing these conditions. The reduction in pituitary–adrenal activity is due to various factors including a suppression of the secretion of corticotropin from the pituitary (indicating a modulated central nervous system response to stress) and reduced adrenal output which ensures in effect a reduction in the plasma concentration of corticoids during lactation. In contrast we have demonstrated that the lactating female is hypersensitive to stimuli emitted by her pups. The lactating mother is more responsive than non-lactating females when the pups are disturbed, either by shocking or simply by handling.

Early in development, shock and handling are not differentiated by the mother; and she responds equally to both of these conditions imposed on her pups. However, later in development, she continues to respond vigorously in terms of pituitary–adrenal activity to shocked pups but not to pups which are handled. Possibly early in development the pups emit equally strong signals regardless of the treatment imposed on them, or conversely, the mother is incapable at that time of discriminating between different stimuli. It appears, therefore, that the buffering of the stress response provides a condition whereby the mother filters out irrelevant stimuli which would normally arouse her. This allows her sensitivity to specific stimuli related to the pups to change. These stimuli now become more arousing and cause the mother to give greater attention to the offspring, particularly in conditions where her offspring are in distress, thereby ensuring the survival of more offspring in the litter.

These data are also pertinent to the understanding of mother–infant interactions. The prevalent view of these interactions focuses more on the phenomenon of the mother imposing certain kinds of controls over the infant. However, mother–infant relationships are dyadic. Interest is growing in the way the infant controls its mother's behaviour. Research on rodents has indicated that the signals emitted by the young influence the behaviour of the mother (Bell et al. 1974; Noirot 1972; Smotherman et al. 1974) and our data indicate that specific stimuli emitted by the young when they are exposed to noxious stimuli arouse the mother. This arousal may point to the mechanism by which the infant controls the mother. Thus, the infant appears to be living in a contingent environment in which it can control outcomes through the specific responses it emits. Seligman (1975) has discussed the problem of 'helplessness', which he defines as the state of an organism in a situation in which it is without any control over outcomes. This organism will not be able to perform appropriately when it needs to regulate and control many aspects of the environment.
Watson (1967) and Seligman (1975) have proposed that the infant is involved in a contingency analysis of the relationship between his responses and their outcomes. The vast amount of information on maternal deprivation, both in animals and in humans, bears witness to the potent and profound effect of maternal deprivation on the subsequent ability of animals to perform adaptively or, to use another term, 'cope'. One of the most important dimensions of coping is control. We propose that the infant, very early in development, learns to control its environment by developing contingent relationships between its responses and the outcomes which are, at this early stage, usually a modification of maternal behaviour. Animals who do not learn control early in development as a consequence of having no potential for these contingency relationships show many indicators of an inability to cope later in life.

In our research on the lactating female rat and pituitary responsiveness we did not set out to try to gain information on the problem of control and contingency relationships but we believe that our results support this model of mother–infant relationships since the signals emitted by the infant appear to be particularly effective in modifying the mother's physiological and behavioural responses.

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