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Cytokines, Infections, Stress, and Dysphoric Moods in Breastfeeders and Formula feeders

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Objective: To analyze relationships between stress, moods, and immunity in breastfeeding compared to formula-feeding mothers.

Design: A cross-sectional study of 181 healthy mothers, exclusively breastfeeding or formula feeding, studied at 4 to 6 weeks after childbirth.

Setting: Mothers were recruited in the postpartum unit of the hospital and then visited in their homes once at 4 to 6 weeks after childbirth for data collection.

Main Outcome Measures: Stress, mood, infection symptoms, and serum levels of interferon-gamma and interleukin-10 were measured.

Results: Formula-feeding mothers had evidence of decreased interferon-gamma and a decreased serum Th1/Th2 ratio (interferon-gamma/interleukin-10) when perceived stress, dysphoric moods, and negative life events were high, an effect consistent with depression of cellular immunity. However, women who were breastfeeding did not show these relationships.

Conclusions: The data suggest that breastfeeding confers some psychoneuroimmunological benefit to mothers, perhaps through prolactin or hypothalamic-hypophyseal-adrenocortical axis stress refractoriness. *JOGNN, 35,* 599-607; 2006. DOI: 10.1111/J.1552-6909.2006.00083.x

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Postpartum women are unique in that they are recovering from birth, have an endocrine profile dependent upon breastfeeding status, and are restoring immunity to normal Th1 (cellular)/Th2 (humoral) balance after profound shifts during pregnancy. They are subject to significant mood changes, with 10% to 15% at risk for serious depression (O'Hara & Swain, 1996). Evidence supports that the postpartum period may be extremely stressful for mothers, and many experience extreme fatigue. Yet, most mothers successfully nurture and protect their fragile infants throughout this vulnerable time. Does nature provide postpartum mothers with benefits that protect from deleterious effects of stress on immunity? And does that benefit extend to a protection against infections in the postpartum period? Does lactation impact stress-immune relationships? These questions have rarely been raised.

Stress was operationalized in this study as scores on a negative life events scale and a perceived stress scale (PSS). Mothers reported on perceived stress and life events that have occurred since the birth of the baby, as well as perceived stress "right now" on the day of measurement. Dysphoric moods were operationalized as the scores on the subscales of the Profile of Mood States (POMS) for depression, anxiety, and fatigue, as well as the total mood disturbance score (TMDS).

Immunity was operationalized as the Th1/Th2 serum cytokine balance as this approach has been used in many stress-immune studies. Cytokines are small messenger molecules released by many cells, including immune cells. They can act very locally, or at small and large distances, and usually require a receptor in order to cause an effect in another cell or tissue. Th1 and Th2 cytokines are released by T helper lymphocytes as well as other cell types. Th1 cytokines help to provide cellular immunity against intracellular bacteria, fungi, and many viruses. Th2 cytokines contribute to humoral immunity, providing protection against extracellular bacteria,

multicellular parasites, some viruses, and many soluble toxins. They are also involved in allergy and autoimmune diseases. Signature cytokines of the Th1 type include interferon-gamma (IFN-γ), and of the Th2 type include interleukin-10 (IL-10). An additional measure of immunity was occurrence of postpartum infection symptoms. This was operationalized by scores on an infection symptom checklist.

The aims of this study were to determine whether stress and dysphoric moods were related to the Th1/Th2 cytokine profile and infection symptoms in postpartum women and whether breastfeeding status affected these relationships. Stress, dysphoric moods, and Th1 (IFN-γ) and Th2 (IL-10) serum cytokines and the Th1/Th2 (IFN-γ/IL-10) ratio were measured. Relationships between stress, dysphoric moods, and reports of symptoms of infection were also studied.

Effects of Stress on Immune Function

Many studies support relationships between stress and immunity. A meta-analysis of more than 180 studies found common effects of stress and depression to be (a) increased white blood cell count, (b) increased cytotoxic natural killer (NK) cell counts and CD8 cells, (c) decreased T cell numbers and increased CD4/CD8 ratio, (d) decreased T cell and NK cell function, and (e) increased leukocyte adhesiveness (Zorilla et al., 2001). According to Padgett and Glaser (2003), over 150 studies have shown relationships between stress, immune function, and impaired health. Many of the stress-immune effects are thought to be due to glucocorticoids, such as in humans, the hormone cortisol, which is released from the adrenal cortex when stimulated by pituitary adrenocorticotrophic hormone (ACTH). In general, stress reduces the Th1/Th2 cytokine balance, an effect of glucocorticoids being suppression of the Th1 axis (Elenkov, 2004). Stress-immune relationships have not been characterized in postpartum mothers, who are recovering from a suppressed Th1 axis during pregnancy, which is presumed to occur as a protection against rejection of the fetal allograft, and are restoring their Th1/Th2 balance to nonpregnancy levels.

Decreased Stress Responsivity in Lactation

There is a decreased physiological responsiveness of the stress response in animal mothers (Shanks, Kusnecov, Pezzone, Berkun, & Rabin, 1997; Windle et al., 1997), but this has not been easily demonstrated in humans. It may be that the stress axes are less responsive only during actual suckling, rather than there being a generally blunted stress response. Laboratory stress paradigms suggest that lactating women do not have an attenuated hypothalamic-hypophyseal-adrenocortical (HPA) response to stress compared to nonlactating postpartum women and controls (Altemus et al., 2001). However, in women tested with a laboratory stress, suckling was associated with attenuated cortisol, ACTH, epinephrine, and norepinephrine release in the feeding condition but not in the holding condition (Heinrichs et al., 2001). Carbon monoxide challenge was used as a stressor in another study (Kaye, Soothill, Hunt, & Lightman, 2004). Suckling produced a short-term suppression of cortisol, but lactating women produced the same stress response as formula feeders and controls to this challenge. The blunted stress response during human lactation may thus depend upon frequency of feeding and on significance of the stressor. Women who are breastfeeding have lower depression and other dysphoric moods, such as *depression, fatigue, and anxiety*; less perception of stress; and more positive life events than formula feeders (Groer, 2005). Breastfeeding appears protective of negative moods and stress, suggesting a resistance against naturalistic and chronic stress in postpartum mothers. Postpartum mothers, and women who are breastfeeding particularly, compared to controls, have an upregulated inflammatory response system, which may protect mothers from infectious disease (Groer et al., 2005).

Stress and Immunity in the Postpartum Period

Few studies are available on stress and immunity in the postpartum period. One report suggested that lactation in rats altered effects of conditioned stress on mesenteric lymph node and splenic lymphocyte proliferation. Lactating animals also produced higher levels of IL-6 after stress exposure (Shanks et al., 1997). Since suckling in human mothers produces relaxation, stress reduction, and a feeling of well-being, the science of psychoneuroimmunology (PNI) provokes a logic question as to whether these positive maternal responses are favorably associated with immune mechanisms. This is particularly of interest because the postpartum period is a highly stressful time in life (Groer, Davis, & Hemphill, 2002), fatigue is a major factor and may affect immune processes (Groër, Davis, Short, & Groër, 2005), and postpartum women are at risk for a variety of dysphoric mood disorders and symptoms (Beck & Indman, 2005). Can breastfeeding in any way ameliorate potential immune effects of negative moods and stress?

Research Questions

The first research question was, "Are postpartum maternal stress and dysphoric moods correlated with IFN-γ, IL-10, IFN-γ/IL-10 balance, and reports of infection symptoms?"; second, "Do exclusively breastfeeding differ from formula-feeding mothers in stress-immune-infection relationships?"

Method

The study was approved by appropriate institutional review boards, and women were recruited in the postpartum unit of the university hospital in a southern

U.S. city. Exclusion criteria were ages less than 18 or greater than 45 years; serious complications during pregnancy, labor, or delivery; chronic mental or physical illnesses; and medications known to influence immune function. There was an effort to overrecruit women from lower socioeconomic groups.

Potential participants were approached before discharge from the hospital after the birth of their full-term infant. Participants were required to read English or Spanish. Spanish language versions of all instruments were available for use with Hispanic mothers, although very few actually enrolled in the study.

The target sample size was 100 in each group based on a power analysis for a medium effect size at the 0.05 level of significance. While 300 mothers were recruited and agreed to participate in the early postpartum period, 181 were retained to collect data at 4 to 6 weeks (mean 5.2 weeks). This 2-week interval was chosen as it reflects a time of transition for new mothers, recovery from the physiological stressors associated with birth and involution, and the appearance of postpartum depression.

Some mothers chose not to participate because of lack of interest, but the major reason that a participant was not retained is that she had begun to supplement and was therefore no longer an exclusive breastfeeder. Mothers were required to be exclusively breastfeeding or formula feeding from birth. All participants received a monetary gift for their time. Assumptions made for this study were that mothers were able to comprehend the instruments and completed all self-report data honestly. Another assumption was that the mothers were essentially healthy and not suffering from any major physical illnesses.

Mothers were visited once in their homes by a nurse researcher, between morning hours of 8 a.m. to 11 a.m. during postpartum weeks 4 to 6, and all data were collected at that time. While efforts were made to collect samples between 8 a.m. and 9 a.m., there were many mothers who lived hours away from the university, and it was difficult for research assistants to collect these samples before 9 a.m. The morning hours were chosen because hormones were measured in the blood samples, some of which were circadian dependent, although these values are not presented in this report. The instruments were sent ahead and mothers completed them on the day of data collection. Mothers were instructed to feed the baby as usual before the visit. The time of last feeding was always within 3 hours of data collection, so no mother was actively suckling the infant during blood collection. A venipuncture was performed into sterile vacutainers. The serum tube was placed on ice and samples were immediately transported to the laboratory.

Cytokines

Interferon-gamma and IL-10 were measured in sera. The cytokines were measured using sandwich enzyme linked immunosorbent assay (ELISA) kits from eBioscience (San Diego, CA). The plates were read at the appropriate wavelengths on a Scantron plate reader, and data were further analyzed using the Prism GraphPad program. The inter- and intraassay coefficients of variation were less than 10%.

Instruments

Demographic data were collected by questionnaire. Symptoms of infection were collected through the Carr Infection Symptom Checklist (Carr SCL) (Table 1). The Carr SCL, developed by the investigators, consists of 30 symptoms, ranked according to severity on a 0- to 4-point Likert scale. There are respiratory, gastrointestinal (GI), genitourinary (GU), skin/eye, and general flu subscales. Scores are computed for both symptom frequency and severity. The scale was originally developed for a study of stress and infection in the menstrual cycle (Groer, Carr, & Younger, 1993). The Carr SCL has been tested in over 400 female participants (including the nearly 200 participants in the current study) and during different seasons to control for seasonal differences in infection risk. A factor analysis with varimax rotations of these data found a five-factor solution that accounted for 48% of variance. Factor loadings indicated high loadings of appropriate symptoms on respiratory, GU, and GI subscales. Cronbach's alpha for the respiratory subscale was 0.87; for skin/eye, .40; for GU, .43; for GI, .55; and for flu, .45. Since respiratory symptoms tend to cluster together (e.g., coughs, runny nose, sneezing), this subscale internal consistency is higher than those of the other scales, which consist of widely disparate items. For example, the skin/eye subscale includes items such as skin rash and stye and the GU includes vaginal discharge and painful urination.

The stress and mood instruments were chosen based on their ability to quantify stressful life events since the baby was born, perception of stress both at the time of testing and over the period since the baby was born, and a range of dysphoric moods that postpartum mothers often experience.

Perceived Stress Scale. The PSS (Cohen, Kamarck, & Mermelstein, 1983) is a 14-item scale that assesses cognitions and emotions related to perceived general stress. The items indicate the degree to which respondents find their lives unpredictable, uncontrollable, and overloading—constructs thought to be central components of the stress experience. There is a 5-point Likert scale response format with options ranging from *never* (0) to *very often* (4), and the scale has a range of 0 to 56. The scale was used in two ways in this study. One version of the scale inventoried stress perceptions since the baby was born, and the other version asked for "today" perceptions. The congruent and criterion validity for the scale has been reported to be excellent (Cohen et al., 1983), although the predictive validity falls with time. Cronbach's alpha for this scale in this study was .84 when the scale was used to measure

TABLE 1
Carr Infection Symptom Checklist©

Have you had any of the following symptoms since the baby was born? If you know symptoms are due to allergy and not infection, do not check.

Please check the correct answer:

0 = No symptoms
1 = Mild symptoms
2 = Moderate symptoms
3 = Strong symptoms
4 = Severe symptoms

	0	1	2	3	4
Cold sores					
Canker sores					
Nasal stuffiness					
Sore throat					
Sinus drainage					
Sinus pain/pressure					
Swollen glands					
Diarrhea					
Abdominal cramps					
Burning on urination					
Dark, smelly urine					
Earache					
Hoarseness					
Styes					
Runny nose					
Skin infections					
Acne					
Red eyes					
Vaginal itching					
Vaginal yeast infection					
Vaginal herpes					
Fever					
Finger nail infection					
Wheezing					
Cough					
Shingles					
Generalized flu-like					
Breast infection					
Episiotomy infection					
Dental abscess					

stress since the baby was born and .88 for stress today. The Cronbach's alpha has been reported to range from .84 to .86 in other studies (Cohen et al.).

Inventory of Small Life Events. The Inventory of Small Life Events (ISLE) (Zautra, 1996) measures minor, daily, negative, and positive events in a person's relationships with friends, spouses, and family. According to Zautra, chronic stress is produced by exposure to everyday small, recurrent, uncontrollable, and unwanted life events. This is stress within the natural occurrences of everyday life or "naturalistic" stress. The scale used here is a minor modification of the scale, developed in consultation with Zautra. It lists 77 events, and participants indicate how many times they have experienced each event since the baby was born. It is scored by adding the number of times each event was experienced. Cronbach's alpha for the ISLE in this study was .81. Others who have used this scale have not reported data on internal consistency reliabilities.

Profile of Mood States. The POMS (McNair, Lorr, & Droppleman, 1992) is a 65-item measure of distressful moods that has been used frequently in research studies. Mothers were asked to report on their moods over the entire time period since the baby was born. The usual way that the POMS has generally been used is to report on feelings over the past week, but it has been used to measure moods over shorter and longer periods (McNair et al., 1992). Experience of mood is reported on a 5-point Likert scale, with responses ranging from 0 (*not at all*) to 4 (*extremely*). It utilizes a 0- to 4-point Likert scale for items that describe ranges of moods, from low to high. Six mood subscales are available. The validity of the scale (face validity, factorial validity, predictive validity, and construct validity) is reported to be excellent (McNair et al.). The internal consistency ranges from .87 to .92 and test-retest reliability from .68 to .74 (McNair et al.). A TMDS is also calculated. The POMS was deemed ideal and valid for assessing a range of common moods experienced by postpartum women. In this study, the TMDS Cronbach's alpha was .95. For the subscales, the following were the Cronbach alphas: depression, .97; anger, .96; fatigue, .89; and anxiety, .89.

Statistical Methods

The data were examined for normality, skewness, and kurtosis. Extreme high outliers in cytokine levels (six outliers in IFN-γ concentrations, which were likely the result of measurement error) were removed from analysis. Cytokine means required log10 transformation in order to achieve normality so that parametric procedures could be used for analysis. Pearson product-moment correlations were used to determine relationships. The *t* tests were used to compare groups. Linear regression was employed to analyze relationships between stress, mood, feeding type, and symptoms of infection. Separate hierarchic regressions were performed for each cytokine and for the ratio of IFN-γ/IL-10. The only demographic variable that correlated with any of the cytokine measures was a correlation between income and serum IFN-γ (r = .21, p < .04). Income and marital status differed between the feeding groups, so these data were entered first into regression equations. Age was entered and found to have

no influence on the results. Feeding status was entered next, then the stress or mood variable, and an interaction term last. Interaction terms between feeding and stress measures and feeding and moods that were correlated with the cytokines were used in these regression models.

Results

Demographic Characteristic

Table 2 shows the demographics of the formula-feeding compared to breastfeeding mothers. Statistically significant differences are indicated. Even though there was an attempt to recruit and enroll an equivalent sample of breastfeeders and formula feeders, there were still socioeconomic differences between the two groups. Women who were breastfeeding were older, had higher income, and more were married. The presence or absence of nonlegal committed relationships were not queried in this study.

The first research question was, "Are postpartum maternal stress and dysphoric moods correlated with IFN-γ, IL-10, IFN-γ/IL-10 balance, and reports of infection symptoms?" Perceived stress scores, negative life events scores, and dysphoric moods scores were examined for relationships with IFN-γ and IL-10 cytokines and with the Th1/Th2 ratio (IFN-γ/IL-10). Correlation analysis showed relationships between perceived stress, depression, anxiety, anger, negative life events, and serum cytokines in the formula feeders but not in women who were breastfeeding. These data are presented in Table 3.

There were many correlations between symptoms of infection and stress and mood in both breastfeeders and formula feeders. Total SCL correlated with perceived stress today ($r = .26$, $p < .000$) and since the baby was born ($r = .30$, $p < .000$), ISLE scores ($r = .25$, $p < .000$), and with all the dysphoric mood scores on the POMs (TMDS, $r = .37$, $p < .000$). Most of these psychosocial variables correlated with each other.

A multiple regression analysis was conducted to predict SCL severity scores from stress and mood variables. Total negative life events, depression, and perceived stress scores produced a model that accounted for 21% of the variance in SCL, $F(1, 180) = 15.9$, $p < .001$. Feeding status was not related to relationships between stress, mood, and symptoms of infection.

The second research question was, "Do exclusively breastfeeding differ from formula-feeding mothers in stress-immune-infection relationships?" Women who were breastfeeding showed no correlations of serum IFN-γ, IL-10, or the Th1/Th2 ratio with any stress or mood measures. In order to further analyze the relationships between feeding status, stress, mood, and immunity, hierarchic regressions were performed separately on serum IFN-γ, serum IL-10, and on the IFN-γ/IL-10 ratio. None of the regression models provided significant sources of variance in IL-10. Income and marital status did not contribute significantly to the regression equations for any of the models. The variables that predicted significant proportions of the variance in serum levels of IFN-γ and the Th1/Th2 ratio were feeding status, and the interaction between feeding and perceived stress today and perceived stress since the baby was born. The directions of these interactions were such that stressed formula feeders, but not women who were breastfeeding, were more likely to have decreased IFN-γ (see Table 4).

TABLE 2
Demographic Differences Between Women Who Are Breastfeeding and Formula Feeders

Variable	*Breastfeeders*	*Formula Feeders*
Income (%)		
<$10,000**	13.6	39.4
>$40,000**	42	9.6
Marital status (%)		
Single*	17	39.4
Married*	79.5	55.3
Divorced	1.1	3.2
Work (%)		
Not working	66	73.4
Part time	11.4	7.4
Full Time	20.5	17
Race** (%)		
White	89.8	73.4
African American	2.3	7.4
Hispanic	3.4	—
Asian	3.4	1.1
Age (years)	28.4*	23.2
Length of labor (hr)	9.76	8.87

*$p < .05$.

**$p < .001$.

> Stressed formula feeders, but not women who were breastfeeding, were more likely to have decreased cellular immunity.

With regard to the relationship between feeding status, stress, and infection symptoms, women who were

TABLE 3
Pearson Correlation Coefficients Between Stress, Dysphoric Moods, and Cytokines in Formula Feeders

Variable	*IFN-γ*	*IL-10*	*IFN-γ/I10*
IL-10	*ns*		
IFN-γ/IL-10	.71***	–.42***	
PSS "today"	–.31**	*ns*	–.34**
PSS "since baby was born"	–.41**	*ns*	–.39**
POMS depression	–.24*	*ns*	*ns*
POMS anxiety	*ns*	*ns*	*ns*
POMS fatigue	*ns*	*ns*	*ns*
POMS anger	–.24*	*ns*	*ns*
POMS vigor	.25*	*ns*	*ns*
TMDS	–.24*	*ns*	–.27*
Negative life events	–.25*	*ns*	*ns*

Note. IFN-γ = interferon-gamma; IL-10 = interleukin-10; PSS = perceived stress scale; POMS = Profile of Mood States.

*$p < .05$.

**$p < .01$.

***$p < .001$.

breastfeeding had significantly lower frequency and severity scores than formula feeders on most of the subscales. Respiratory symptoms comprised the majority of reports (Table 5). Forward regression analysis found that feeding and negative life events accounted for 10% of the variance in respiratory symptoms (adjusted $R^2 = .104$, $p = .000$). Respiratory infection symptom reports were significantly correlated with stress and mood in formula feeders (see Table 6).

Discussion

The stressors experienced by formula-feeding postpartum women appear to have the potential to depress cellular immune competence, while women who were breastfeeding may be protected from deleterious influences of stress on immunity. The effects of stress and mood are not large, in that only a small proportion of the variance in serum cytokines could be accounted for by stress, feeding status, or interactions between feeding status and stress. Clearly, a large number of factors not measured explain the remaining variance. The interaction terms entered into the regression equations suggest that stressed formula-feeding mothers were more likely to have lower IFN-γ and a lower Th1/Th2 ratio. Serum cytokines such as IFN-γ reflect multiple cellular sources, uptake by receptors throughout the body, and the influence of dynamic and multiple neuroendocrine and metabolic factors. Protection from stress-related decreases in cellular immunity in breastfeeding mothers and lack of equivalent protection in formula feeders suggests that there is some risk for the latter group. Nevertheless, these effects are quite small in postpartum mothers. The clinical effects of these

TABLE 4
Regression Analyses on Serum Interferon-Gamma

	R	R^2	*Change in* R^2	*Standardized Beta*	t
Perceived stress since the baby was born					
Marital status	.05	.003	–.002	–.097	–1.28
Income	.08	.006	–.002	.056	0.787
Feeding	.08	.007	.000	.36	2.26*
PSS	.129	.017	.01	–.116	–1.72
Feeding × PSS	.214	.046	.03	–.408	–2.62**
Perceived stress today					
Marital status	.052	.003	.003	–.055	–0.641
Income	.08	.006	.004	.072	–0.908
Feeding	.086	.007	.001	.391	2.27*
PSS today	.143	.02	.013	–.131	–1.8
Feeding × PSS today	.241	.06	.038	–.466	–2.76**

Note. PSS = perceived stress scale.

*$p < .05$.

**$p < .01$.

TABLE 5
Scores of Subscales on the Carr Infection Symptom Checklist

	*Respiratory**	*Skin/Eye**	*Gastrointestinal**	*Genitourinary**
Breastfeeders (n = 86)	2.71 ± 4.2 (range 0-23)	0.97 ± 1.35 (range 0-6)	1.33 ± 2.14 (range 0-11)	1.4 ± 1.7 (range 0-8)
Formula feeders (n = 92)	3.73 ± 3.9 (range 0-16)	1.47 ± 1.9 (range 0-9)	0.80 ± 1.66 (range 0-11)	1.84 ± 0.18 (range 0-8)

*$p < .05$.

relationships may translate into postpartum illness, but this was not evident in the mothers' retrospective recall of symptoms of infections. Other illnesses potentially affected by an alteration in the Th1/Th2 balance were not measured in this study.

While there is equivocal evidence about the degree and nature of diminished stress reactivity in lactating women, our previous work suggests that humans are unique in that postpartum mothers differ in the HPA axis, dysphoric moods, naturalistic stress responses, and immune and inflammatory processes compared to nonpostpartum control women (Groër et al., 2005). In the current report, exclusively breastfeeding and formula-feeding mothers were studied on relationships between naturalistic stressors, dysphoric moods, symptoms of infection, and serum cytokine levels. The data suggest potentially diminished cellular immunity in formula-feeding postpartum mothers experiencing stress. This is in line with many PNI studies, which show stress and depression suppression of cellular immunity (Zorilla et al., 2001). Glucocorticoids are thought to be the primary mechanisms for Th1 suppression in stress states (Elenkov, 2004). Glucocorticoid-mediated pathways may involve inhibition of nuclear factor kappa B (NF-κB) translocation, which is involved in release of many cytokines. Another factor is prolactin. Breastfeeding mothers have much higher levels of prolactin than formula feeders, and prolactin is known to stimulate pathways leading to Th1 activation (Dimitrov, Lange, Fehm, & Born, 2004; Meli et al., 2003). Prolactin is related to positive mood and decreased stress in both breastfeeders and formula feeders (Groer et al., 2005). Prolactin may be another pathway by which Th1 cytokines are preserved during stress in women who were breastfeeding.

More precise markers such as cytokine RNA message and longitudinal methods as well as experimental approaches will help answer questions that arise from the data. Clinical relationships of the serum cytokine balance to symptoms of infectious illness in these complex human postpartum mothers were not apparent. Nevertheless, the interaction between stress and cellular immunity in formula-feeding women, which was independent of demographic factors, suggests that these women are potentially at risk.

TABLE 6
Correlations Between Respiratory Symptoms and Mood and Stress

Mood and Feeders Stress Variable	*Women Who Are Breastfeeding* r	*Formula Feeders* r
POMS fatigue	*ns*	.26**
POMS anxiety	*ns*	.31**
Negative life events	.31**	.20*

Note. POMS = Profile of Mood States.

*$p < .05$.

**$p < .01$.

This research suggests that the stress and dysphoric moods experienced by some mothers have the potential to influence their immune balance.

Limitations

This research was cross sectional and nonexperimental and thus suffers many limitations related to the type of data that is collected in this approach. All the demographic, psychosocial, and infection data were self-reported, and the study would be strengthened by the collection of more objective health data in particular. It is also likely that these instruments did not capture the unique aspects of postpartum stress and mood. Exclusivity of breastfeeding status was also by self-report and may not always have been precise. Breastfeeding and formula-feeding groups were not demographically equivalent, which is another limitation of the study. It cannot be determined from this study whether inherent and unique personality traits might be present in the feeding groups as well, which could

account for the differences in stress and dysphoric moods, as well as in immune characteristics. Other illnesses not measured may have been present and might have altered the immune response (STDs, autoimmune diseases, etc.).

Clinical Implications

While nature generally seems to protect and favor postpartum mothers, this research suggests that the stress and dysphoric moods that are experienced by some mothers have the potential to influence their immune balance. Mothers most at risk are formula-feeding mothers when measured at this point of time in the postpartum period. Protective immunity is obviously of great importance, considering that mothers are the first line of defense for their newborns, and maternal immune status protects the health of the infant. Breastfeeding is the natural and evolutionarily beneficial mode of feeding for all animal species, including humans. No other organism can actually *choose* not to lactate except for humans. The immune vulnerabilities uncovered in the study were experienced by formula feeders, and not women who were breastfeeding, suggesting that formula-feeding mothers lack some protective influence inherent in breastfeeding. What these protections might be is not yet known but nurses should recognize at least some potential for psychoneuroimmunological effects of stress in postpartum mothers, particularly if they do not breastfeed.

> Nursing should promote breastfeeding as the preferred feeding method and promote good hygiene, adequate sleep, and good nutrition to prevent infection.

This research supports nursing's effort to promote and protect breastfeeding as the preferred method for feeding infants in almost every situation. It also serves to alert nurses to the possibility that formula-feeding mothers might be at higher risk for certain illnesses. Infection symptom reports are generally higher in formula feeders. Other possible manifestations of a changing Th1/Th2 immune balance, not measured in this study, could include allergies, autoimmune diseases, and even malignancies. Nurses caring for mothers and infants along the perinatal and postpartum trajectory have many opportunities to influence the stress-immune relationships reported here. Helping mothers to recognize stressful stimuli, their unique psychophysiological responses to stress, and ways to cope with stress are important interventions. The sources of stress are multiple, from interpersonal to role (Groer et al., 2002), and mothers can be helped to recognize that these stressors can be anticipated. Postpartum mothers may even experience posttraumatic stress from the stress of birth (Beck, 2004).

While the data reported here suggest that formula-feeding mothers appear more vulnerable, parity and demands of parenting may also be important. Recent research suggests that multiparous formula-feeding mothers are at a higher risk for abnormal salivary cortisol rhythms, suggesting dysregulation of the HPA axis (Tu, Lupien, & Walker, 2006). The demands of parenting the new infant and multiple siblings are sources of stress and may lead to dysphoric moods. The postpartum mother and her partner may be able to better handle this type of stress by interventions that help participants to evaluate and develop their parenting skills (Misri, Reebye, Milis, & Shah, 2006). Encouraging mothers to seek help and support when feeling sad, or anxious, and helping mothers to ward off fatigue may deflect more serious dysphoria. Because of the potential for immune decrements in stressed formula-feeding mothers, there should be special attention by the nurse to educate mothers about hygiene, sanitation, infection transmission, healthy diet, and adequate sleep. The mother's state of health will also directly impact her new infant's health, and this point should be emphasized in planning care.

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