Immune Responses in Mothers of Term and Preterm Very-Low-Birth-Weight Infants

SUSAN GENNARO,1*, WILLIAM P. FEHDER,2 AVITAL CNAAN,2,3 RUTH YORK,1 DONALD E. CAMPBELL,2,4 PAUL R. GALLAGHER,3 AND STEVEN D. DOUGLAS2,4

University of Pennsylvania School of Nursing,1 Division of Immunologic and Infectious Diseases, Department of Pediatrics2 and Department of Biostatistics,3 University of Pennsylvania School of Medicine, and Clinical Immunology Laboratory, Joseph Stokes Jr. Research Institute, and Children’s Hospital of Philadelphia,4 Philadelphia, Pennsylvania

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Differences in the levels of immune cell subsets present in peripheral blood have been demonstrated based on sociodemographic factors such as age and race. Postpartal women, who are recovering from the immune changes that are concomitant with pregnancy, have lymphocyte and monocyte values that differ from other populations. A subgroup of postpartal women, mothers who deliver preterm very-low-birth-weight (VLBW) (∼1,500 g) infants, may have further differences in values of immune cell subsets and in immune functioning either because of hormonal factors or lifestyle changes or because of the stress they experience after their infant’s birth and for the first few months of infant caretaking. This study examined anxiety, depression, and immune cell phenotypes in 30 mothers of VLBW infants and in 30 mothers of healthy term infants over the first 4 postpartal months to determine if mothers of preterm VLBW infants differed from mothers of healthy term infants in psychological and immunologic parameters. Additionally, lymphocyte proliferation and natural killer cell functional assays were performed in a subset of mothers. Mothers of VLBW infants had increased anxiety and decreased lymphocyte proliferation compared to mothers of term infants. When lymphocyte and monocyte subsets were compared over time between the two groups of mothers differences were found in CD4, CD20, CD3+/CD56+, CD14, and HLA class II a on monocytes. Mothers with high-fat diets had lower percentages of some monocytes (CD14), lymphocytes (CD4+/CD5RA+), and natural killer cells (CD3+/CD57+) during the first 4 postpartal months.

Sociodemographic factors such as age, gender, and race are known to contribute to differences in the levels of monocyte and lymphocyte subsets present in peripheral blood (31, 36). Not surprisingly, therefore, postpartal mothers of term infants, who are recovering from immune changes concomitant with pregnancy, differ from men and nonpostpartal women in immune cell phenotypes during the first 4 postpartum months (18). A subgroup of women, mothers who deliver preterm (<37-week-gestation), very-low-birth-weight (VLBW) (∼1,500 g) infants may, because of lifestyle or hormonal changes or stress, have further differences in the levels of immune cell subsets and in immune functioning than do mothers of healthy term infants.

Stress may influence both the quantity and functioning of immune cell subsets (20). Anxiety and depression have also been related to decreases in the number of circulating monocytes (20) and natural killer (NK) cells (10, 11) in a wide range of circumstances (widowers [2, 5], pregnant women [21], divorcees [27], and caretakers of elderly Alzheimer’s patients [26, 28]). The initial unstable health of VLBW and preterm infants and the long hospitalization required before they are able to go home has been related to increased anxiety and depression for their mothers both during infant hospitalization and after hospital discharge (3, 16). Infant well-being continues to be a concern for the mother through the first few months of the infant’s life as the baby’s health fluctuates widely in this period (22). Approximately 30% of VLBW infants require rehospitalizations during their early months of life (33, 39).

Even those infants who have a relatively smooth course require complex caretaking at home that may include apnea monitoring, the administration of multiple medications, and increased contact with health care providers (4). Therefore, mothers of preterm VLBW infants and mothers of healthy term infants may differ in the amount of stress they experience.

Motherhood causes changes in lifestyle which may also influence immune response. Mothers of young infants may skip meals because of time constraints or from a desire to return to prepregnancy weight (19). In nonpostpartal populations dietary imbalances, including inadequate protein (7) and increased fat (30), have been associated with depressed immune function (1, 6, 30). Mothers, once they are no longer pregnant, may increase their amount of cigarette smoking (34), which may be related to decreased immunity by damaging respiratory and vascular tissues or interacting with metabolism and micronutrient intake (9). We have compared immune cell subsets, immune function, anxiety, depression, nutrition, and smoking behaviors in mothers of preterm VLBW infants and mothers of healthy term infants over the first 4 postpartal months to determine if these two groups of postpartal women differ in psychologic and immunologic status.

MATERIALS AND METHODS

Subjects. The study was performed with 60 postpartal women. Thirty women had preterm VLBW infants, and 30 had healthy, normal-weight term infants. Postpartal mothers of term infants were selected so that their age, socioeconomic status, parity, and race were comparable to the mothers of the VLBW infants (Table 1). No mother of a term infant who was ill or septic or who had respiratory difficulties, congenital anomalies, or asphyxia was included in the study. Additionally, women were excluded from the study who had chronic medical and psychiatric problems, any known infection including human immunodeficiency virus (HIV) infection, or a recent pregnancy (less than 1 year before this study). Mothers who delivered very-low-birth-weight infants (<1,500 g) were eligible for the study. Mothers of healthy, normal-weight term infants (37-week-gestation) were enrolled to serve as controls. Mothers of infants born at any gestation lower than 37 weeks who met study criteria were also eligible.

* Corresponding author.

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and complete blood counts and differential analyses were performed with a
tensity reliability was 0.82 for anxiety and 0.81 for depression.
portant to study multiple markers of NK cell populations, e.g., CD3
blood. After incubation for 30 min at 4°C, 2 ml of lysing buffer, maintained at
fluorochrome-conjugated monoclonal antibody was added to 0.1 ml of whole
(13).
Mothers of term infants
[58x337]and complete blood counts and differential analyses were performed with a
[58x257]Anxiety Inventory (17, 37). In the present study the internal consis-
[147x273]/CD56
[150x697]SD
[207x309]/CD29
[220x716]a
[242x686]No. black No. white Mean (SD) Median No. unmarried No. married
[247x276]1
[272x257]/CD16
[292x260]1
[316x309]the51Cr released from lysed cells. Total release activity was determined by 51Cr
fluid was removed at appropriate time points (in triplicate) for the evaluation of
achieved appropriate effector cell to target cell ratios. The plates were centrifuged
plates, which was followed by the addition of serially diluted effector cells to
achieved 50% of the isotype from labeled target cells. Spontaneous release was
[316x333]and incubated for 4 h (K562 cell targets). One-tenth of a milliliter of supernatant
[316x358]titer plates, which was followed by the addition of serially diluted effector cells to
[316x366]in 5% CO2 with gentle agitation, the cells were washed four times and resus-
[316x374]of Na2
[316x390]rapidly thawed cryopreserved target cells were washed and resuspended in 0.2 ml
of Hanks’ balanced salt solution and labelled with 51Cr by the addition of 50 μCi of
[316x382]and incubated for 4 h at 37°C in 5% CO2 with gentle agitation, the cells were washed four times and resus-
[316x374]106 cells. After a 1-h incubation at 37°C
[433x260]3
[491x431]unstimulated cpm).
[501x171]t test, after a log

### Table 1. Maternal demographic characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean age ± SD (yr)</th>
<th>Race</th>
<th>Annual income ($)</th>
<th>Marital status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mothers of VLBW infants</td>
<td>25 ± 6.7</td>
<td>19</td>
<td>20,529 (25,311)</td>
<td>21</td>
</tr>
<tr>
<td>Mothers of term infants</td>
<td>25 ± 6.3</td>
<td>19</td>
<td>16,280 (19,309)</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>25 ± 6.5</td>
<td>38</td>
<td>18,478 (22,530)</td>
<td>41</td>
</tr>
</tbody>
</table>

*There were no statistically significant differences for any of the demographic characteristics between the groups.

*Mean birth weight, 1.136 ± 0.274 g.

*Mean birth weight, 3.452 ± 0.578 g.

### Immunologic studies.
Peripheral venous blood was obtained from mothers, and complete blood counts and differential analyses were performed with a Coulter STKS (an automated cell counting and flow cytometric scatter analysis system) (Coulter Electronics, Hialeah, Fla.). Additionally, cell phenotypes were determined including CD3 (pan T cell), CD4 (helper T cell), CD8 (suppressor, cytotoxic T cell), CD11b (IC83 receptor), CD4+CD29+ (a CD4-positive lymphocyte marker), CD4+CD56+ (NK cell), CD4+CD56+ (CD16+ and CD16−), CD5+ (NK cell) and CD3+CD57 (NK cell marker). The decision to transform values, and nutrition variables were compared by using a log transformation to reduce skewness when necessary. The decision to transform was based on histogram results. In the cases where transformed values were used, the geometric mean on the original scale is given as well as the median absolute deviation estimator since the standard deviation on the original scale is not an appropriate measure of spread. Repeated measures analysis of variance models were fit to the mental state variables, leukocyte data, immunologic markers, and health behaviors to examine whether the two groups changed over time and whether the pattern of change over time was similar or different between the two groups, above and beyond any baseline differences. The models used the actual time since delivery in the fit, and both linear and quadratic time effects were fit. The choice of whether to use the quadratic fit or only the linear term depended on the significance of the quadratic coefficients, and the size of the residuals. Leukocyte responses in vitro were analyzed similarly.
TABLE 2. Mental state and immunologic parameters at delivery

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean score or % positive ± SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mothers of VLBW infants</td>
<td>Mothers of term infants</td>
</tr>
<tr>
<td>Anxiety</td>
<td>7.17 ± 3.75</td>
<td>4.57 ± 2.93</td>
</tr>
<tr>
<td>Depression</td>
<td>12.67 ± 6.21</td>
<td>10.50 ± 4.30</td>
</tr>
<tr>
<td>T-cell marker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD8</td>
<td>16.57 ± 10.33</td>
<td>21.49 ± 8.26</td>
</tr>
<tr>
<td>CD4</td>
<td>46.57 ± 9.82</td>
<td>46.09 ± 12.43</td>
</tr>
<tr>
<td>CD29</td>
<td>38.56 ± 16.04</td>
<td>43.21 ± 15.24</td>
</tr>
<tr>
<td>CD11b (lymphocyte)</td>
<td>5.26 ± 4.36</td>
<td>8.11 ± 6.51</td>
</tr>
<tr>
<td>Ia (lymphocyte)</td>
<td>13.00 ± 6.40</td>
<td>15.69 ± 7.09</td>
</tr>
<tr>
<td>CD3</td>
<td>79.98 ± 7.50</td>
<td>82.42 ± 6.87</td>
</tr>
<tr>
<td>CD45RA</td>
<td>36.56 ± 18.53</td>
<td>43.01 ± 16.77</td>
</tr>
<tr>
<td>Monocyte marker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD11b</td>
<td>77.45 ± 31.61</td>
<td>92.62 ± 10.47</td>
</tr>
<tr>
<td>CD14</td>
<td>81.06 ± 14.39</td>
<td>91.74 ± 7.75</td>
</tr>
<tr>
<td>Ia</td>
<td>76.95 ± 29.61</td>
<td>88.96 ± 14.16</td>
</tr>
<tr>
<td>B-cell marker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD20</td>
<td>5.00 (2.75–9.88)</td>
<td>7.61 (5.65–12.10)</td>
</tr>
<tr>
<td>NK cell marker</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD3/CD16*</td>
<td>2.64 (1.50–5.05)</td>
<td>4.22 (2.65–7.45)</td>
</tr>
<tr>
<td>CD3/CD56*</td>
<td>3.74 (2.00–7.25)</td>
<td>6.11 (3.50–11.20)</td>
</tr>
<tr>
<td>CD3/CD57*</td>
<td>1.77 (0.95–3.10)</td>
<td>2.08 (1.30–4.15)</td>
</tr>
</tbody>
</table>

* Values for B-cell and NK cell markers are geometric means (interquartile ranges are shown in parentheses).

RESULTS

(i) Comparisons at delivery. There were no statistically significant differences between the mothers of the VLBW infants and the mothers of the term infants for any of the demographic variables (Table 1). All leukocyte parameters were compared by using a t test after a natural log transformation to reduce skewness. There were no significant differences between the two groups.

A summary of the mental state variables and the immunologic parameters at delivery is given in Table 2. The mothers of VLBW infants had higher anxiety (P = 0.004) but not higher depression (P = 0.12) immediately following delivery compared with the mothers of term infants. Mothers of VLBW infants had lower levels of CD8 at delivery (16.6%) than did mothers of term infants (21.5%) (P = 0.05). The percentages of CD11b on lymphocytes was 5.3 and 8.1% for mothers of VLBW and term infants, respectively (P = 0.055). There were also differences in CD20 levels, a B-cell subset, which were lower in mothers of VLBW preterm infants than in mothers of term infants (P = 0.036) (geometric means, 5.0 and 7.6, respectively).

The three monocyte markers (CD14, Ia, and CD11b) were either significantly or borderline higher in the mothers of term infants than in mothers of VLBW infants. The percentages of NK cells was significantly higher for both CD3~/CD16~ and CD3~/CD56~ in mothers of term infants (P = 0.04 and P = 0.03, respectively) but were not different for CD3~/CD57~.

(ii) Longitudinal comparison of anxiety, depression, and immunologic markers. Repeated measures models were fit to all parameters (Table 3). The P value represents whether the changes over time were similar or different between the mothers of VLBW infants and the mothers of term infants (interaction effect) above and beyond differences at delivery. Group differences (in anxiety and time differences (CD4~/CD29~, CD11b lymphocytes, and total activated T cells) are discussed below but are not shown in Table 3.

The results for mothers of VLBW infants showed statistically significant differences in anxiety compared with the results for mothers of term infants (P = 0.0096). Anxiety continued to be higher in mothers of VLBW infants than in mothers of term infants at every data point and did not significantly change over time until 4 months postpartum in either group (P = 0.63). There were no significant differences in depression between the two groups, and similar to anxiety, levels stayed the same across time.

There were no significant differences in total leukocyte counts between mothers of VLBW infants and mothers of term infants (P = 0.70). Both groups of mothers started out at essentially the same point (10.4 × 10⁴ cells for the VLBW group versus 11.0 × 10⁴ cells for the term group), which dropped quickly over time (P < 0.00005) so that by the first postpartum month the leukocyte counts were 6.2 and 6.1, respectively, for mothers of VLBW and of term infants. Both groups had the same pattern of change over time (P = 0.16) with no further changes occurring after the first postpartum month.

Both the mothers of VLBW infants and the mothers of term infants started out at essentially the same percentage in lymphocytes, but the mothers of VLBW infants ended at a slightly lower percentage than the mothers of term infants, with the groups having changed at a different rate across time (P = 0.0002). Neutrophil levels also were similar at delivery but decreased at a slower rate in mothers of VLBW infants than in mothers of term infants (P = 0.006). Eosinophils increased more in the mothers of term infants than in mothers of VLBW infants (P = 0.001).

For all the T-cell markers, the quadratic model provided a better fit than the linear model. In most parameters this reflected a phenomenon of decreased values at delivery and an increase by 1 month postpartum. This increase was sustained, in most cases throughout the 4-month period, although in some cases, there was a decrease by the 4-month measure-
ment. Among the T-cell markers, CD8 levels showed differences between groups over time, with CD8 percentages in mothers of VLBW infants increasing to levels comparable to those of mothers of term infants by 1 month and to higher levels at 2 and 4 months (P = 0.005) (Fig. 1).

The percentages of CD4+/CD29+ were lower at delivery than they were later in the postpartal period in both groups (average of 41% at delivery that increased by 4 months postpartum to 52%; P < 0.0027). The percentages of total activated T cells (CD3+/CD57+) also increased over time (average of 10.15 at delivery versus 12.45% at 4 months; P = 0.0001). This pattern of comparably lower rates at baseline for mothers of VLBW infants and mothers of term infants rising to comparably higher levels at 4 months postpartum also held true for CD11b receptor-bearing lymphocytes (5.3% in mothers of VLBW infants and 8.1% in mothers of term infants; P = 0.0025), CD3, CD4, CD4+/CD45RA+, and Ia on lymphocytes showed no differences, either at delivery or at later datum points, between the two groups.

A linear model fit the monocyte marker data well. At delivery the percentage of CD14+ was 10.15 at delivery versus 12.45% at 4 months; P = 0.0001. The percentages of CD4+/CD16+ continuously increased from delivery to 4 months (P = 0.0005 for most comparisons). CD56+ demonstrated different patterns across time. While percentage of CD56+ increased over the 4-month period than the mothers of term infants. The mothers of VLBW infants showed a quicker rate of increase than the mothers of term infants. The NK function decreased faster in the mothers of VLBW infants increasing to levels comparable to mothers of healthy term infants rising to comparable higher levels at 4 months postpartum also held true for CD11b receptor-bearing lymphocytes (5.3% in mothers of VLBW infants and 8.1% in mothers of term infants; P = 0.0025), CD3, CD4, CD4+/CD45RA+, and Ia on lymphocytes showed no differences, either at delivery or at later datum points, between the two groups.

(iii) Lymphocyte proliferation and NK cell assays. Lymphocyte responses in vitro and NK functions were assessed in five randomly chosen mothers in each group, at all time points. In most cases the lymphocyte responses were lower in the VLBW mothers than in the term mothers (P < 0.005 for most comparisons) (Table 4).

In NK functional activity, there were no differences between mothers of term infants and mothers of VLBW infants at delivery. The mean chromium release at dilutions of both 50 and 25 showed differences across time (P < 0.00005 and P = 0.03, respectively). The NK function decreased faster in the
VLBW mothers than in the term mothers. This result was also observed at one more dilution (12.5) (P = 0.054). However, because of the small sample size, these results should be interpreted cautiously and an assessment of magnitude of effect is not reliable at this point.

(iv) Postpartal health behaviors: smoking and nutrition. There were no differences between the two groups of mothers attributable to smoking behavior. When smoking was examined to determine if it had an effect on the immune profile (by using cotinine level as a covariate in the repeated measures analysis), only one of the immune parameters from Table 3 showed any significance, and this was marginal, especially in light of the large number of parameters being examined. There were no statistically significant differences between mothers of term infants and mothers of VLBW infants in protein, calorie, or fat intake.

Nutritional status was related to immune function in the postpartal women. Although there were no differences between mothers of VLBW infants and mothers of term infants in total calories, the percentage of calories that were obtained from protein, or the percentage of calories ingested from protein or fat intake, at any of the data points, there was a significant difference between women with high-fat and normal fat diets in CD3/CD57 percentages (an NK subset) (P = 0.01) at delivery. At 2 months there were significant differences between mothers with high-fat and normal fat diets in CD14 (monocyte) (P = 0.02) and CD4/CD45RA percentages (inducer-suppressor) (P = 0.02), with women with high-fat diets having lower percentages at each data point.

**TABLE 4. Differences in lymphocyte proliferation assays**

<table>
<thead>
<tr>
<th>Mitogen</th>
<th>Mean lymphocyte proliferation (cpm) ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHA 24h</td>
<td>Mothers of VLBW infants</td>
</tr>
<tr>
<td>1.0</td>
<td>125 ± 15</td>
</tr>
<tr>
<td>2.5</td>
<td>125 ± 15</td>
</tr>
<tr>
<td>9.0</td>
<td>125 ± 15</td>
</tr>
<tr>
<td>25.0</td>
<td>125 ± 15</td>
</tr>
<tr>
<td>PWM 24h</td>
<td>Mothers of VLBW infants</td>
</tr>
<tr>
<td>1.0</td>
<td>125 ± 15</td>
</tr>
<tr>
<td>2.5</td>
<td>125 ± 15</td>
</tr>
<tr>
<td>9.0</td>
<td>125 ± 15</td>
</tr>
<tr>
<td>25.0</td>
<td>125 ± 15</td>
</tr>
<tr>
<td>ConA 24h</td>
<td>Mothers of VLBW infants</td>
</tr>
<tr>
<td>1.0</td>
<td>130 ± 15</td>
</tr>
<tr>
<td>2.5</td>
<td>130 ± 15</td>
</tr>
<tr>
<td>9.0</td>
<td>130 ± 15</td>
</tr>
<tr>
<td>25.0</td>
<td>130 ± 15</td>
</tr>
</tbody>
</table>

**FIG. 1.** CD8 percentages at delivery and at 1, 2, and 4 months after delivery for mothers of VLBW infants and mothers of term infants. Values are means, and 95% confidence intervals are shown (error bars).
haps dietary influences on NK cell functioning overrode any difference that might have been observed between mothers of term infants and mothers of VLBW infants in NK cell response to stress.

Women with low-protein, low-calorie diets had significantly lower percentages of CD3+/CD57+ (NK cell subset) at delivery \( (P = 0.007) \) as well as significantly lower percentages of CD4+/CD29+ (inducer-helper T-cell subset) \( (P = 0.03) \). At 2 months postpartum women with low-calorie and low-protein diets had significantly lower percentages of CD11b lymphocytes \( (P = 0.01) \), and at 4 months postpartum, women with low-protein, low-calorie diets had significantly lower levels of total activated T cells \( (P = 0.004) \) and Ia on lymphocytes \( (P = 0.01) \).

**DISCUSSION**

The leukocytosis of pregnancy is due primarily to a granulocytosis \( (8) \). This granulocytosis was comparable in both the mothers of VLBW infants and mothers of term infants and returned to baseline by the first postpartal month. The changes in the level of total leukocytes may be related to cortisol levels, catecholamine, or other endocrine factors or leukotrenes in pregnancy. While there have been several studies of lymphocyte subsets and mitogenic responses during pregnancy, here-tofore there have been no investigations of the role of a major stressor, the delivery of a VLBW infant, on immunologic markers in these women. Mothers of VLBW infants experienced higher anxiety over time which did not resolve until 4 months postpartum. Concomitantly, our data show some decrease in the percentages of lymphocytes and eosinophils. These decreases may be related to stress and increased corticosteroid levels or, perhaps, to estrogen levels.

We also observed important differences between mothers of VLBW infants and mothers of term infants in the expression of Ia on monocytes, which were reduced at delivery in the mothers of VLBW infants and continued to be reduced at 1 month with recovery at 2 and 4 months. The expression of CD14 on cells gated as monocytes was reduced for the mothers of VLBW infants at delivery, 1, and 2 months and recovered at 4 months. In contrast, CD11b expression on monocytes was not significantly different between mothers of VLBW infants and term mothers. These differences indicate that the changes in the cell surface display of molecules on monocytes may be related to monocyte activation, namely Ia and CD14. CD14 is a major receptor for lipopolysaccharide on monocytes \( (41) \). There are several possible interpretations of these observations. One is the possibility that altered expression of CD14 and Ia in the absence of changes in CD11b levels (the complement receptor) reflect a response of monocytes to stress, namely caring for a VLBW preterm infant. Another possibility is that there is a shift in the composition of circulating monocyte populations and that these differ between mothers of term infants and mothers of VLBW infants. A recent study has shown diminished expression of CD14 on neonatal monocytes and neutrophils \( (35) \). Furthermore, the expression of these receptors may be altered by steroid, endocrine, or other serum-derived factors in mothers of VLBW infants. For example, although most women did not breastfeed, differences in prolactin levels may have contributed to differences between the groups.

Some postpartal changes in subsets of T cells which have been reported by others, such as a decline in CD4 accompanied by an increase in CD8 and a postpartal increase in CD4+/CD45RA+ \( (38) \), were not found in this study. CD4 levels and CD4+/CD45RA+ levels remained stable in both groups of mothers. Inducer-suppressor cells (CD4+/CD45RA+) \( (32) \) may have an important role in postpartum immune dysfunction such as postpartal thyroiditis \( (38) \). CD4+/CD45RA+ cells are also elevated in patients with certain primary immune deficiencies such as chronic mucocutaneous candidiasis \( (29) \).

Although CD8 levels did rise in mothers of VLBW infants, it actually decreased in mothers of term infants. The levels of CD8 at delivery (mothers of VLBW infants, 16%; mothers of term infants, 21%) and at 4 months postpartum (22% in both groups of mothers) were relatively low compared to the work of Stagnaro-Green and colleagues \( (38) \), who reported CD8 levels of 30.5 and 31.3% at 3 and 6 months postpartum for a group of normal postpartum women. The basis for these differences may be related to the monoclonal antibody used, the flow cytometry gating techniques, or demographic features of the population studied.

The mothers in our study were primarily from a lower socioeconomic background, and health behaviors such as poor nutrition and lack of exercise may have had an effect on immune profiles in both the mothers of VLBW infants and the mothers of term infants, which make comparisons difficult between this sample of mothers and more advantaged postpartal women. Differences between the mothers of VLBW infants and the mothers of term infants within the study were controlled methodologically by matching mothers of VLBW infants and mothers of term infants on parity, age, socioeconomic level, and race, and no statistical differences were found between groups when lifestyle variables were controlled (see Table 1). Therefore, we are confident that differences between the two groups of mothers in immune profiles cannot be attributed to differences in lifestyle variables. Without a nonpostpartal control group of women matched for age, race, and socioeconomic status it is difficult to know if these nutritional inadequacies are unique to the postpartal period or if they are related to other factors such as socioeconomic status. For both mothers of term infants and mothers of VLBW infants who are poor, inadequate nutrition may decrease the number of peripheral blood lymphocytes, monocytes, and NK cells present.

The poorer lymphocyte proliferative response to PHA, ConA, and PWM demonstrated by mothers of VLBW infants compared to mothers of term infants is very likely to be indicative of a stress response \( (23) \). At each of two dilutions for three different mitogens mothers of VLBW infants continually demonstrated less proliferative responses. This supports earlier findings of decreased lymphocyte responses in stressed individuals \( (26) \).

In studies of men with human immunodeficiency virus, severe stress was associated with reductions in NK cell populations and in CD8 counts, T cells which are related to cytotoxic effector T cells \( (12, 13) \). The results of our studies are consistent with the stress-related alterations in these subsets but further analysis is necessary, especially analysis that controls for endocrine changes.

The mothers of VLBW infants in this study experienced increased anxiety, decreased lymphocyte proliferation, and decreased percentages of some immunologic cell subsets during the first 4 postpartal months compared to mothers of healthy term infants. The postpartal period is a time when the immunosuppression associated with pregnancy is still resolving, and mothers of preterm, VLBW infants appear to differ from mothers of healthy term infants in immune status in the early postpartal period.

**ACKNOWLEDGMENT**

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