Plasma leptin influences gestational weight gain and postpartum weight retention\(^1-3\)

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ABSTRACT

Background: Leptin, a product of the obese \(\text{ob}\) gene, is released from adipocytes. At the same body mass index, women have higher concentrations than men. Thus, during pregnancy, leptin may influence gestational weight gain and retention of a portion of that gain postpartum.

Objective: We examined the relation between plasma leptin at entry to prenatal care and subsequent changes in weight from entry to prenatal care (at 17 wk gestation, baseline) until 6 mo postpartum.

Design: This was an observational study of leptin, gestational weight gain, and postpartum weight retention (at 6 wk and 6 mo postpartum) in 103 low-income pregnant women from Camden, NJ, with a pregravid body mass index (in kg/m\(^2\)) in the normal range (19.8–26).

Results: After potential confounding variables were controlled for, leptin at entry significantly \((P < 0.05)\) predicted weight gain in pregnancy, including measured rate of weight gain \((\bar{x} \pm \text{SEE}: 0.25 \pm 0.13 \text{ kg} \cdot \text{unit log leptin}^{-1} \cdot \text{wk}^{-1})\), measured rate of third-trimester weight gain \((0.37 \pm 0.15 \text{ kg} \cdot \text{unit log leptin}^{-1} \cdot \text{wk}^{-1})\), rate of weight gain from recalled pregravid weight \((0.23 \pm 0.09 \text{ kg} \cdot \text{unit log leptin}^{-1} \cdot \text{wk}^{-1})\), and net rate of gestational weight gain \((0.22 \pm 0.09 \text{ kg} \cdot \text{unit log leptin}^{-1} \cdot \text{wk}^{-1})\). The leptin concentration at entry also significantly predicted retained weight in the postpartum period (at 6 mo: 7.29 \pm 3.33 kg/unit log leptin at entry) and marginally predicted changes in the sum of skinfold thicknesses (at 6 mo: 14.7 \pm 7.5 mm/unit log leptin at entry).

Conclusion: These results suggest that a high leptin concentration at entry to prenatal care may predict an increased risk of overweight and obesity in vulnerable women. *Am J Clin Nutr* 1998;68:1236–40.

KEY WORDS  Leptin, pregnancy, gestational weight gain, postpartum weight, skinfold thickness, females

INTRODUCTION

Leptin, a recently (1994) discovered polypeptide hormone, is a product of the obese \(\text{ob}\) gene and is the first hormone found to be released from adipocytes (1, 2). Leptin acts on the hypothalamus, the site of appetite regulation in the brain. In the \(\text{ob/ob}\) mouse the absence of leptin induces obesity by increasing dietary intake. In female mice, leptin reduces infertility by decreasing dietary intake, body weight, and fat mass (3). Administration of leptin to normal mice increases energy expenditure and advances the onset of sexual maturation (4).

In humans, leptin correlates positively with body fat content and body mass index (BMI); in addition, it responds to and may be regulated by circulating insulin. Although plasma concentrations of leptin generally rise with increasing adiposity, there is a sexual dimorphism in its regulation for males and females at the same level of fatness or BMI. Females have plasma leptin concentrations that are 1.5–3-fold higher than those of males (5, 6). These findings suggest a differential resistance to the action of leptin that may have adaptive significance for reproduction. As a result, the potential exists for leptin to influence factors such as weight gain during the course of pregnancy and retention of pregnancy gain into the postpartum period.

On average, women gain \(\geq 12.5\) kg during pregnancy, most of which is lean tissue and water but that also includes \(\approx 3.5\) kg fat (7). Some women gain considerably more weight, and thus accrue additional fat (8). Excessive weight gain during pregnancy that began in 1985. The site of the study—Camden, NJ—is one of the poorest cities in the United States (13). The study was approved by the Human Studies Institutional Review Board of the University of Medicine and Dentistry of New Jersey. Women with serious nonobstetric problems (eg,
The 103 subjects included in this analysis were a subsample of 274 pregnant women aged 13–29 y followed to 6 mo postpartum (14, 15) with a pregravid BMI in the normal range (19.8–26.0) as defined by the Institute of Medicine (15). Subjects with samples available for leptin assay at entry to prenatal care and at either week 28 of gestation or at 6 wk postpartum were included. Their characteristics were similar to those of the underlying group contributing the original data (Table 1). The exception was maternal age, which was somewhat greater for included women than for the women not included.

Subjects were seen at entry to prenatal care (=17 wk gestation; interquartile range: 13–22 wk), early in the third trimester at week 28, at 6 wk postpartum, and at 6 mo postpartum. At each of the first 3 visits, a blood sample was taken, centrifuged (22,500 × g, 10 min, 4°C), and the plasma stored at −70°C until assayed. The plasma was analyzed for leptin with a kit marketed by Linco Research Inc (St Charles, MO). All analyses were run in duplicate.

Socioeconomic, demographic, anthropometric, and dietary data, as well as information on gestation duration, pregnancy complications, and outcome were obtained as described previously (13, 14). Briefly, maternal weight was measured at each visit, height was measured at entry to prenatal care, and pregravid weight was obtained by recall. Skinfold thicknesses (triceps and subscapular) were measured at entry, 28 wk gestation, and 6 wk and 6 mo postpartum as outlined previously (16). Twenty-four–hour dietary recalls were obtained at entry to prenatal care and week 28. Energy intakes from these 2 recalls were averaged.

Our principal gauge of weight gain was a measured rate of gain based on maternal weights taken between 20 and 36 wk gestation, with the rate representing the average (kg/wk) increments from 20 to 24, 24 to 28, 28 to 32, 32 to 34, and 34 to 36 wk. A measured rate of weight gain during the third trimester, computed as the difference between measured weights at week 28 of gestation and at delivery were also used.

We also used rate of weight gain based on recalled pregravid weight. This definition of gestational weight gain was computed as the difference between pregravid weight and weight at delivery to yield a total weight gain. Net weight gain was computed as the difference between total weight gain and infant birth weight. Rate of weight gain was computed by dividing total gain and net weight gain by gestation duration estimated from the mother’s last menstrual period.

The recalled pregravid weight is the variable most often used to estimate weight gain during pregnancy (15). Studies have shown consistently that weight is reliably recalled (r > 0.9), except by overweight individuals, who tend to systematically underestimate measured weight (17, 18). In Camden, the correlation between measured weight (second trimester) and recalled weight was similar (r > 0.9) (19, 20). BMI was computed as weight at entry to prenatal care (in kg) by height squared (in m). Because BMI at entry to prenatal care included part of the total pregnancy weight gain, total weight gain in pregnancy was par-

### Table 1

<table>
<thead>
<tr>
<th>Variable Included</th>
<th>Not included</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>18.8 ± 0.39</td>
</tr>
<tr>
<td>BMI based on recalled pregravid weight (kg/m²)</td>
<td>22.8 ± 0.32</td>
</tr>
<tr>
<td>BMI at study entry (kg/m²)</td>
<td>24.2 ± 0.35</td>
</tr>
<tr>
<td>Gestational age at entry (wk)</td>
<td>17.1 ± 0.51</td>
</tr>
<tr>
<td>Sum of skinfold thickness at entry (mm)</td>
<td>37.0 ± 1.10</td>
</tr>
<tr>
<td>Total weight gain in pregnancy (kg)</td>
<td>14.2 ± 0.72</td>
</tr>
<tr>
<td>Measured rate of weight gain (kg/wk)</td>
<td>0.54 ± 0.027</td>
</tr>
<tr>
<td>Measured rate of net weight gain (kg/wk)</td>
<td>0.28 ± 0.018</td>
</tr>
<tr>
<td>Measured rate of weight gain in third trimester (kg/wk)</td>
<td>0.58 ± 0.032</td>
</tr>
<tr>
<td>Weight gain rate based on recalled pregravid weight (kg/wk)</td>
<td>0.36 ± 0.018</td>
</tr>
<tr>
<td>Retained weight at 6 wk postpartum</td>
<td>5.52 ± 0.73</td>
</tr>
<tr>
<td>Retained weight at 6 mo postpartum</td>
<td>4.52 ± 0.73</td>
</tr>
<tr>
<td>Average energy intake during pregnancy (kJ)</td>
<td>9286 ± 400.1</td>
</tr>
</tbody>
</table>

Gestation duration (%)

- `
≥ 37 wk` | 89.3% [92] | 92.9% [158]

Birth weight (%)

- `
≥ 2500 g` | 88.3% [91] | 93.5% [159]

Parity (%)

- `Primiparous` | 62.1% [64] | 58.8% [100]
- `Multiparous` | 37.9% [39] | 41.2% [70]

Ethnicity (%)

- `Black` | 59.2% [61] | 61.2% [104]
- `Non-Black` | 40.8% [42] | 38.8% [66]

Smoking status

- `Nonsmoker` | 74.8% [77] | 74.7% [127]
- `Smoker` | 25.2% [26] | 25.3% [43]

Notes:

- `n` in brackets.
- `± SEM`.
- `Significantly different from included, P < 0.05.`
tiated from BMI at entry and a residualized BMI score was used for each individual. Postpartum retained weight was defined for 2 time spans: pregravid to 6 wk postpartum and pregravid to 6 mo postpartum.

Multiple regression analysis was used to assess the independent effects of leptin (normalized by using a log transformation) at baseline after 7 potential confounding variables were controlled for: age, parity, ethnicity, BMI at entry to prenatal care (residualized by weight gain), sum of skinfold thicknesses (triceps and subscapular) at entry to prenatal care, smoking status, and gestation at blood draw. Both lactation status and measured rate of weight gain during pregnancy were used as control variables in the postpartum analyses. The SAS statistical package (SAS Institute, Cary, NC) was used for statistical analyses.

RESULTS

Mean (±SEM) plasma leptin concentrations increased significantly as pregnancy progressed from the first measurement point at entry to prenatal care (baseline: 19.0 ± 1.0 μg/L) to 28 wk gestation (22.6 ± 1.1 μg/L, P < 0.05). By early postpartum (6 wk), plasma leptin concentrations had declined below baseline (15.6 ± 1.0 μg/L, P < 0.05). During pregnancy, subjects gained 14.2 ± 0.72 kg by the time of delivery, with an average measured rate of weight gain of 0.54 ± 0.03 kg/wk. Weight retention averaged 5.5 kg at 6 wk postpartum and 4.5 kg at 6 mo postpartum (Table 1).

Pregravid BMI was not correlated with rate of weight gain during pregnancy, regardless of how it was measured. For example, the correlation with measured rate of weight gain (r = 0.01; n = 103) was small and not significant. Average energy intake (9286 ± 400 kJ) during pregnancy was not consistently correlated with rate-of-weight-gain measures. Of these, only the measured rate of weight gain showed a marginal correlation with average energy intake during pregnancy; however, it was not significant (r = 0.17, P < 0.09; n = 103).

At entry, in bivariate analyses, plasma log leptin was associated with several background characteristics potentially related to gestational weight gain and postpartum retained weight (Table 2). Smoking status was associated with lower leptin concentrations, whereas BMI at entry, the sum of skinfold thicknesses (triceps and subscapular) at entry, and primiparity were positively associated with initial leptin concentrations. Initial log leptin was unrelated to gestation at entry (Table 2). Likewise, there was no correlation between log leptin at entry and average energy intake (r = 0.00, NS; n = 103).

The more detailed multiple regression analysis showed that, after potential confounding variables were controlled for, gestational weight gain and postpartum retained weight increased as baseline leptin concentrations increased (Tables 3 and 4). There was a positive and linear relation between the log leptin concentration at entry and measured rate of gestational weight gain, rate of weight gain based on recalled BMI, as well as net rate of gestational weight gain. After the sum of skinfold thicknesses at entry to prenatal care was controlled for, each of the above relations persisted. Additional control for average energy intake during pregnancy did not alter these results.

For example, for each unit increase in log leptin, the measured rate of weight gain increased by 0.25 kg/wk (Table 3). Thus, during pregnancy, a woman with a baseline concentration of leptin in the 90th percentile might be expected to have a measured weight gain of 0.45 kg/wk compared with 0.31 kg/wk for a woman with a leptin concentration in the 10th percentile. As a result, during an average gestational period for this sample (38.8 wk), women in the 90th percentile for leptin would gain an average of 5.43 kg more by the time of delivery than would women in the 10th percentile.

Entry log leptin also predicted the measured rate of weight gain during the third trimester of pregnancy (b = 0.37, SEE = 0.15 kg/wk, P < 0.05, and adjusted R² = 0.21, where b is the estimated regression coefficient) when BMI at entry, sum of skinfold thicknesses at entry, as well as the other potentially confounding variables (age, parity, ethnicity, smoking status, gestational age at entry, and energy intake during pregnancy) were controlled for.

The leptin concentration at baseline significantly predicted retained weight at 6 wk and 6 mo postpartum. After potential confounding variables were controlled for, including maternal lactation status, there was a positive relation between baseline leptin and weight retention at both 6 wk and 6 mo postpartum. This association persisted after the addition of measured rate of gestational weight gain during pregnancy as a control variable (Table 4). Thus, after adjustment for measured rate of gain and other potential confounding variables, a woman with a leptin concentration in the 90th percentile (29.5 μg/L) at entry would be expected to retain an additional 13.9 kg beyond her pregravid weight at 6 mo postpartum. In contrast, a woman with a leptin concentration in the 10th percentile (8.51 μg/L) at entry would be expected to retain an additional 2.69 kg.

After potential confounding variables included in the weight-retention models were controlled for, maternal lactation status had a marginal independent effect on postpartum retained weight. There was an increase in weight retention for lactators at 6 wk (b = 3.95, SEE = 1.57 kg, P < 0.05) but not at 6 mo (b = 1.88, SEE = 1.66 kg, P < 0.26) postpartum. Changes in the sum of the

<p>| TABLE 2 |
| Relations of background variables with initial log leptin concentrations |</p>
<table>
<thead>
<tr>
<th>Background characteristic</th>
<th>Pearson r or independent groups t test</th>
<th>Higher initial log leptin concentration associated with</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>r = −0.10 [103]</td>
<td>NS</td>
</tr>
<tr>
<td>BMI at entry (kg/m²) residualized by weight gain</td>
<td>r = 0.36 [103]</td>
<td>Higher BMI</td>
</tr>
<tr>
<td>Gestational age at entry (wk)</td>
<td>r = 0.03 [103]</td>
<td>NS</td>
</tr>
<tr>
<td>Sum of skinfold thicknesses at entry (mm)</td>
<td>r = 0.48 [103]</td>
<td>Higher sum of skinfold thicknesses at entry</td>
</tr>
<tr>
<td>Smoking status</td>
<td>t = 2.76 [103]</td>
<td>Nonsmoking status</td>
</tr>
<tr>
<td>Parity</td>
<td>t = −1.85 [101]</td>
<td>Primiparity</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>t = 1.16 [101]</td>
<td>NS</td>
</tr>
</tbody>
</table>

1P < 0.001.
2P < 0.0001.
3P < 0.01.
4P < 0.10.
skinfold thicknesses from entry to 6 mo postpartum showed a marginally significant positive relation with entry log leptin concentrations when variables in the weight-retention model were controlled for. This amounted to an estimated increase of 14.7 mm in the sum of skinfold thicknesses at entry to 6 mo postpartum per unit log leptin at entry to prenatal care ($b = 14.7$, $SEE = 7.49$ mm, $P < 0.053$).

### DISCUSSION

Women who have a pregravid BMI within normal limits, but who have elevated plasma leptin concentrations at baseline are predisposed to greater weight gains during pregnancy and to more weight retention postpartum; obesity may be a consequence for some in the long term.

There was an effect of leptin on gestational weight gain even after adjustment for other variables that correlated with leptin concentrations, including the sum of skinfold thicknesses at entry and BMI at entry. In this study, apart from BMI and the sum of skinfold thicknesses at entry, smoking status and gestational age at entry were controlled for.

#### TABLE 3
Baseline leptin concentrations as a predictor of weight gain (kg/wk) during pregnancy

<table>
<thead>
<tr>
<th>Weight retention at 6 wk postpartum</th>
<th>Log leptin concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>$b$</td>
<td>6.64$^2$</td>
</tr>
<tr>
<td>SEE</td>
<td>3.14</td>
</tr>
<tr>
<td>Adjusted $R^2$</td>
<td>0.34</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weight retention at 6 mo postpartum</th>
<th>Log leptin concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>$b$</td>
<td>7.29$^2$</td>
</tr>
<tr>
<td>SEE</td>
<td>3.33</td>
</tr>
<tr>
<td>Adjusted $R^2$</td>
<td>0.36</td>
</tr>
</tbody>
</table>

$^1$Age, parity, BMI at entry (residualized by weight gain), smoking status, sum of skinfold thicknesses at entry, and gestational age at entry were controlled for.

$^2$P < 0.05.

### REFERENCES


