

## **Blood lead levels increase, but remain in normal range with severe weight reduction.**

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## Blood lead levels and bone turnover with weight reduction in women

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High bone turnover states are known to raise blood lead levels (BPb). Caloric restriction will increase bone turnover, yet it remains unknown if weight reduction increases BPb due to mobilization of skeletal stores. We measured whole blood Pb levels (<sup>206</sup>Pb) by inductively coupled plasma mass spectrometry in 73 women (age 24–75 years; BMI 23–61 kg/m<sup>2</sup>) before and after 6 months of severe weight loss (S-WL), moderate weight loss (M-WL), or weight maintenance (WM). Baseline BPb levels were relatively low at 0.2–6.0 µg/dl, and directly associated with age ( $r = 0.49$ ,  $P < 0.0001$ ). After severe WL ( $-37.4 \pm 9.3$  kg,  $n = 17$ ), BPb increased by  $2.1 \pm 3.9$  µg/dl ( $P < 0.05$ ), resulting in BPb levels of 1.3–12.5 µg/dl. M-WL ( $-5.6 \pm 2.7$  kg,  $n = 39$ ) and WM ( $0.3 \pm 1.3$  kg,  $n = 17$ ) did not result in an increase in BPb levels ( $0.5 \pm 3.2$  and  $0.0 \pm 0.7$  µg/dl, M-WL and WM, respectively). BPb levels increased more with greater WL ( $r = 0.24$ ,  $P < 0.05$ ). Bone turnover markers increased only with severe WL and were directly correlated with WL. At baseline, higher calcium intake was associated with lower BPb ( $r = -0.273$ ,  $P < 0.02$ ), however, this association was no longer present after 6 months. Severe weight reduction in obese women increases skeletal bone mobilization and BPb, but values remain well below levels defined as Pb overexposure. *Journal of Exposure Science and Environmental Epidemiology* (2008) 0, 000–000. doi:10.1038/jes.2008.5

**Keywords:** blood lead, bone turnover, calcium, severe obesity, weight loss.

### Introduction

Lead is a leading environmental toxicant and Pb exposure has effects on the nervous, cardiovascular, endocrine and immune systems, and reproductive function. Most of the body Pb resides in the skeleton (Barry 1975), which may offer protection to other tissues, but can also be a long-term source of Pb transfer to other tissues under conditions of bone resorption. For example, demineralization of bone in postmenopausal women can increase blood Pb (BPb) levels by 25% (Silbergeld et al., 1988), whereas the high bone turnover associated with pregnancy and lactation increases Pb levels in blood and breast milk (Gulson et al., 2003; Manton et al., 2003). Also, the high bone turnover associated with semi-starvation increases BPb levels in Pb-exposed rats (Han et al., 1999).

Weight loss in human trials has been shown to increase bone turnover (Hyldstrup et al., 1993; Svendsen et al., 1993; Ricci et al., 2001), especially in older individuals and with greater weight reduction. Voluntary caloric restriction typically results in moderate 10% weight reduction, whereas

gastric reduction surgery results in about 30% loss in weight (Balsiger et al., 2000; Coates et al., 2004). We hypothesized that weight reduction would result in bone mobilization and release of Pb into circulation. Understanding how weight reduction affects Pb levels is important in light of the high prevalence of dieting and the increased bone turnover in susceptible populations (i.e., postmenopausal women or in women after surgical weight loss; Ricci et al., 2001; Riedt et al., 2005, 2006). In addition, since a lower level of dietary Ca intake or higher age during weight reduction can exacerbate bone mobilization (Ricci et al., 1998; Jensen et al., 2001), and the influence of these variables on Pb release from bone was also addressed in this study. To our knowledge, no clinical trial has investigated whether the rise in bone turnover associated with weight reduction increases BPb levels.

### Materials and methods

#### Subjects and Protocol

Weight-stable (no change in body weight in past 3 months) women who had been recruited for weight loss and weight maintenance studies within our laboratory from 2002 to 2005 (Riedt et al., 2005, 2006, 2007). Over a period of 6 months, overweight and moderately obese participants were counseled

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by a registered dietitian to either maintain their weight (WM group) or to lose a moderate amount of weight (M-WL) using moderate energy restriction to 1200 to 1500 kcal/day and behavior modification. Severely obese participants had elected to undergo Roux-en-Y gastric bypass surgery for weight loss (S-WL group) in the treatment of obesity. Of those who had consented to participate in this study, complete measurements were collected for 73 women (Caucasian,  $n = 61$ ; African-American,  $n = 9$ ; Hispanic,  $n = 2$ ; Asian,  $n = 1$ ). All applicable institutional and governmental regulations concerning ethical use of human volunteers were followed during this research. The study was approved by Rutgers University Institutional Review Board.

Participants were instructed to consume a Ca supplement. Specifically, the overweight and moderately obese women were randomly assigned in a double-blind manner to receive a daily Ca-citrate supplement (Mission Pharmacal) containing either 0.2 or 1.0 g Ca per day. The Ca supplement and a vitamin/mineral supplement were provided to the overweight and moderately obese women. Compliance was monitored through pill counts. The severely obese women were instructed to independently purchase and consume a Ca supplement (1.2 to 1.5 g/day) and a vitamin and mineral supplement, as part of their dietary intervention after the weight loss surgery. Intake was monitored at least six times during the study period.

### Methods

A beam balance (Detecto, Webb City, MO, USA), electronic scale (ScaleTronix ST 5002, White Plains, NY, USA), and stadiometer (Detecto) were used to measure weight and height to the nearest 0.25 kg and 1 cm, respectively, before and 6 months after weight loss or maintenance.

Fasting blood, serum, and urine was collected at baseline and after 6 months.

Whole blood Pb levels ( $^{206}\text{Pb}$ ) were measured by inductively coupled plasma mass spectrometry (ICP-MS) on a Thermo-elemental X5 instrument (Thermo Fischer Scientific). Briefly, whole blood samples were digested using a microwave sample digester (CEM Mars 2000). Samples were digested in high-purity concentrated nitric acid (Fischer Scientific Optima grade) and diluted to a final acid concentration of approximately 5% with 18 MΩ water. Blood (0.5 ml) was added to 1 ml of acid in a 7-ml Teflon vessel. The blood was digested in the microwave digester using the oyster tissue method, which consists of a ramp to pressure (300 PSI) for 20 min with 100% of 300 W power, pressure is held at 200°C for 10 min. The samples are allowed to cool for more than 30 min, and the method is repeated for solutions that are cloudy or with flocculant. After digestion, samples are diluted to a final volume of 20 ml and then analyzed by ICP-MS using calibration standards (High Purity, Charleston SC). The three primary isotopes

of lead  $^{206}\text{Pb}$ ,  $^{207}\text{Pb}$ , and  $^{208}\text{Pb}$  were monitored and agreement within the isotopes was used as a quality control measure.  $^{206}\text{Pb}$  was used as the quantified isotope.

Bone turnover markers were measured in serum and urine samples. Serum N-telopeptide of type I collagen (sNTx) was measured by ELISA (Osteomark; OSTEON International, WA, USA; CV=4.6%). Serum osteocalcin (OC) was measured by radioimmunoassay (RIA; BTI; MA, USA; CV<9%). Pyridinoline (PYD; CV<8%) and deoxypyridinoline (DPD; CV<10%) were measured in 24-h urine samples by reverse-phase HPLC and fluorescence detection.

Calcium intakes were analyzed from 3-day food records using Nutritionist Pro (version 1.3.36; First Data Bank, CA, USA) at baseline and twice during the 6 months of weight loss. The reported total Ca intakes include dietary as well as supplemental Ca.

### Statistical Analysis

Values are expressed as mean  $\pm$  SD. Overweight and moderately obese women who had lost <2.5% of their initial body weight after 6 months were included in the WM group, and those losing >2.5% of their initial body weight were in the M-WL group. Severely obese women in the S-WL group were analyzed separately. Paired *t*-tests were used to compare baseline to final values. Comparisons of the changes in variables measured between the groups were made using analysis of covariance (ANCOVA), using baseline values of each measured variable to correct for non-normal distribution, and subsequent analysis with Tukeys–Kramer *post hoc* test for unbalanced means was performed if  $P < 0.05$ . Pearson's product–moment correlations were used to examine the relationships between measured variables at baseline, and between the absolute changes in weight, BPb, Ca, and markers of bone turnover. Stepwise multiple regression analysis was performed with changes in BPb as the dependent variable and the changes in weight, Ca variables, and bone turnover markers as independent variables. Analyses were performed with SAS software (version 9.1.3; SAS Institute, Cary, NC, USA). Values were considered statistically significant at  $P < 0.05$ .

### Results

The mean age of the women was  $47 \pm 13$  years (24–75 years) and baseline BMI was  $33.3 \pm 10.6 \text{ kg/m}^2$  (23–61  $\text{kg/m}^2$ ). Baseline characteristics by group are presented in Table 1. Differences between the three groups at baseline ( $P < 0.05$ ) include BMI, body weight, and urinary PYD cross-links. After 6 months, 39 women had lost a moderate amount of weight, 17 women had undergone weight loss surgery, and 17 women had maintained their weight (Table 2).

**Table 1.** Characteristics at baseline and final measurement.

	Weight maintenance, <i>n</i> = 17		Moderate weight loss, <i>n</i> = 39		Severe weight loss, <i>n</i> = 17	
	Baseline	Final	Baseline	Final	Baseline	Final
Age (years)	50.2 ± 12.0		46.4 ± 14.7		46.6 ± 11.3	
Body weight (kg) <sup>a</sup>	72.7 ± 7.7	73.1 ± 7.1	73.7 ± 8.3	68.0 ± 8.2*	132.5 ± 19.3	95.1 ± 14.0*
Blood Pb (µg/dl)	1.4 ± 0.9	1.3 ± 0.7	1.4 ± 1.0	2.0 ± 3.2	1.9 ± 1.4	3.9 ± 3.4*
Calcium intake (mg/day)	1095 ± 435	1308 ± 411	1200 ± 460	1381 ± 504*	1080 ± 455	1141 ± 754
Serum Osteocalcin (ng/ml)	8.2 ± 1.8	8.5 ± 1.7	8.6 ± 1.8	8.2 ± 1.8*	9.2 ± 2.0	12.9 ± 3.1*
Serum NTx (nM BCE)	17.3 ± 6.8	16.3 ± 5.1	14.2 ± 4.1	13.4 ± 3.5	16.3 ± 5.8	26.1 ± 6.5*
Urinary PYD (nM/day) <sup>a</sup>	147.5 ± 74.8	139.3 ± 80.5	175.1 ± 116.6	161.3 ± 114.0	460.6 ± 239.2	811.7 ± 229.5*
Urinary DPD (nM/day) <sup>a</sup>	79.3 ± 37.4	74.8 ± 37.8	69.5 ± 39.6	70.8 ± 43.4	52.7 ± 39.7	124.8 ± 75.1*
Urinary Calcium (mg/day)	176.0 ± 72.8	161.9 ± 97.2	179.9 ± 102.0	163.0 ± 95.4	185.4 ± 97.6	102.5 ± 52.7*

Abbreviations: BCE, bone collagen equivalent; DPD, deoxypyridinoline cross-links; NTx, N-telopeptide of type I collagen; Pb, lead; PYD, pyridinoline cross-links.

<sup>a</sup>Differs among groups at baseline, ANOVA. Different superscripts letters indicate differences between groups (*P* < 0.05).

\**P* < 0.05, values differ from baseline measurement within each group.

**Table 2.** Changes (Δ) in characteristics after 6 months.

	Weight maintenance, <i>n</i> = 17	Moderate weight loss, <i>n</i> = 39	Severe weight loss, <i>n</i> = 17	<i>P</i> -value <sup>1</sup>
Body weight (kg)	0.3 ± 1.3 <sup>a</sup>	-5.6 ± 2.7 <sup>b</sup>	-37.4 ± 9.3 <sup>c</sup>	< 0.0001
Blood Pb (µg/dl)	-0.0 ± 0.7 <sup>a</sup>	0.5 ± 3.2 <sup>a</sup>	2.1 ± 3.9 <sup>b</sup>	0.0416
Calcium intake (mg/day)	212 ± 490	181 ± 443	61 ± 642	0.4781
Serum Osteocalcin (ng/ml)	0.3 ± 2.2 <sup>a</sup>	-0.4 ± 1.2 <sup>a</sup>	3.7 ± 2.5 <sup>b</sup>	< 0.0001
Serum NTx (nM BCE)	-1.0 ± 3.9 <sup>a</sup>	-0.8 ± 4.7 <sup>a</sup>	9.8 ± 4.4 <sup>b</sup>	< 0.0001
Urinary PYD (nM/day)	-8.2 ± 77.3 <sup>a</sup>	-13.7 ± 122.9 <sup>a</sup>	351.1 ± 212.9 <sup>b</sup>	< 0.0001
Urinary DPD (nM/day)	-4.5 ± 44.4 <sup>a</sup>	-1.3 ± 48.6 <sup>a</sup>	72.1 ± 63.3 <sup>b</sup>	< 0.0001
Urinary calcium (mg/day)	-4.6 ± 58.3 <sup>a</sup>	-16.9 ± 77.5 <sup>a</sup>	-83.0 ± 88.3 <sup>b</sup>	0.0070

Abbreviations: BCE, bone collagen equivalent; DPD, deoxypyridinoline cross-links; NTx, N-telopeptide of type I collagen; Pb, lead; PYD, pyridinoline cross-links.

Changes differ among groups, ANCOVA, with baseline characteristics as covariates. Different superscripts letters indicate differences between groups (*P* < 0.05).

### Body Weight and Markers of Bone Turnover

Baseline and final body weight are presented in Table 1. BMI differed (*P* < 0.0001) between the overweight/obese women (28.0 ± 3.4 kg/m<sup>2</sup>) and the S-WL group (50.8 ± 6.8 kg/m<sup>2</sup>) at baseline. At final measurement, women in the M-WL group had lost 7.7 ± 3.7% of their body weight and the S-WL group had lost 28.1 ± 5.5%. The WM group maintained their weight within 0.6 ± 1.9% after 6 months. The S-WL group showed an increase (*P* < 0.001) in all markers of bone turnover. A greater weight loss was accompanied by an increase in markers of bone formation (OC) and bone resorption (sNTx, PYD, and DPD) at final measurement (*r* = -0.495 to -0.726, *P* < 0.0001).

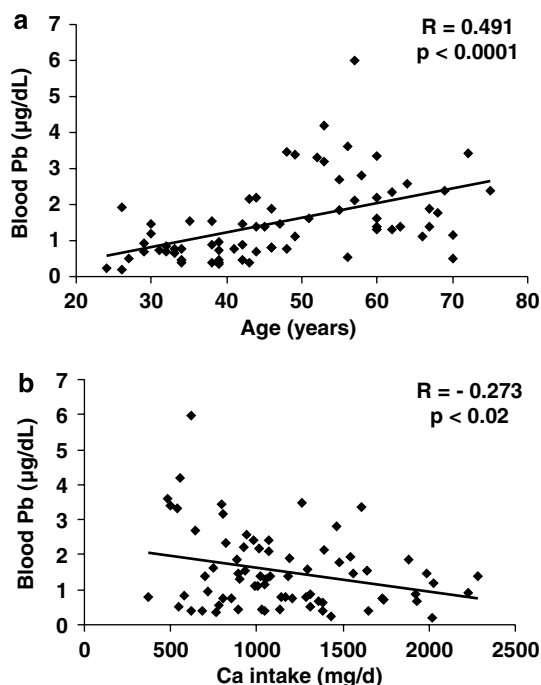
### Blood Lead

BPb levels at baseline ranged from 0.2 to 6.0 µg/dl, and were not different between groups. A correlation between BPb levels and age (*r* = 0.491, *P* < 0.0001) was present at baseline (Figure 1a). Women with a higher Ca intake at baseline had lower BPb levels (*r* = -0.273, *P* < 0.02, Figure 1b). How-

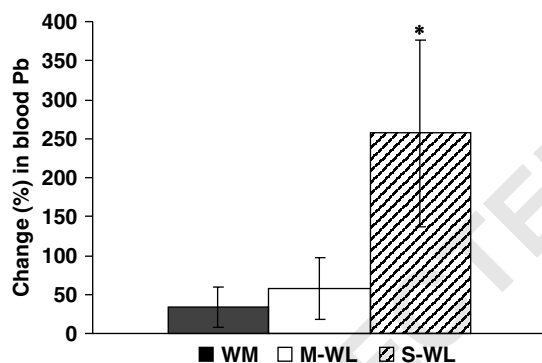
ever, this association was no longer present during caloric restriction at 6 months. BPb levels had significantly increased (*P* < 0.05) with S-WL, and differed (*P* < 0.05) from the M-WL and WM groups (Figure 2). Individual values of BPb for women in the S-WL group are shown at baseline and 6 months after weight loss surgery (Figure 3). Final BPb values ranged from 0.3 to 17.8 µg/dl across all the three groups. A greater increase in BPb levels was associated with greater weight loss and increases in urinary PYD cross-links (Table 3). Stepwise multiple regression analysis showed that changes in PYD explained 8.2% of the variance in BPb changes after 6 months of weight loss (*P* < 0.02, β-estimate: 0.00417).

### Calcium

Total Ca intake at baseline ranged from 366 to 2284 mg/day and from 287 to 2574 mg/day at final measurement, and was not different between the three groups at either baseline or final measurement. Ca intake was not correlated to markers of bone turnover at baseline, but there was a trend for high

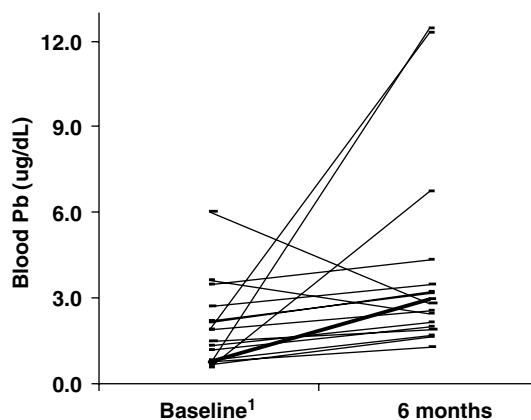


**Figure 1.** Associations between blood Pb levels and age (a) and calcium intake (b) at baseline measurement in 73 overweight and obese women.



**Figure 2.** The change (%) in blood Pb levels from baseline to after 6 months of weight maintenance (WM,  $n = 17$ ), moderate weight loss (M-WL,  $n = 39$ ), and severe weight loss (S-WL,  $n = 17$ ). \* $P < 0.02$ , ANCOVA, differs from M-WL and WM. Values are means  $\pm$  SE. Black column, WM; blank column, M-WL; hatched column, S-WL.

Ca intake to lower PYD levels during caloric restriction ( $P < 0.06$ ,  $r = -0.224$ ). Twenty-four hours urinary Ca excretion did not differ between the groups at baseline, but showed a trend ( $P < 0.06$ ) for a difference between groups at final measurement. A greater urinary Ca excretion was associated with greater Ca intakes ( $P < 0.05$ ,  $r = 0.234$ ) and with lower BPb levels ( $P < 0.05$ ,  $r = -0.264$ ) at the 6-month measurement. Women in the S-WL group were also analyzed in two groups above and below the 50th percentile of Ca intake, and showed no significant difference in the BPb response.



**Figure 3.** Individual responses to BPb values in women with severe weight loss. <sup>1</sup>Woman with baseline Pb value of 6 µg/dl has a low Ca intake ( $\sim 0.6$  g/day) that increases after surgery ( $\sim 1.2$  g/day); all other women have either a recommended baseline Ca intake (1 to 1.2 g/day) or show no change after surgery.

## Discussion

In the current study, we tested the hypothesis that weight loss-induced bone resorption would result in the release of Pb into circulation. In addition, we examined whether dietary Ca intake during weight loss was associated with bone turnover and BPb levels. Understanding how weight reduction affects Pb levels is important in light of the high prevalence of dieting and findings that caloric restriction increases bone turnover in susceptible populations (i.e., postmenopausal women or after surgical weight loss; Ricci et al., 2001; Riedt et al., 2005, 2006). We found that after severe, but not moderate weight loss, BPb levels increase compared to baseline, but are still  $< 13$  µg/dl. The rise in BPb levels could only partially be explained by increases in bone resorption associated with greater weight reduction. Other metabolic and hormonal changes subsequent to surgery may also be important in determining BPb levels. Dietary Ca intake alone is not capable of preventing the rise in bone turnover or BPb levels with severe weight loss.

Weight loss has previously been shown to result in an increase in bone resorption (Ricci et al., 2001; Cifuentes et al., 2004), especially so in women who undergo severe weight loss due to surgery (Coates et al., 2004; Riedt et al., 2006). In Pb-exposed rats, it was shown that weight loss increased BPb levels and organ Pb concentrations (Han et al., 1999). In the current study, BPb levels increased significantly only in the severe weight reduction group, and this is consistent with the rise in bone turnover with severe but not moderate weight reduction. Urinary bone resorption markers were twice as high as after 6 months in women with severe weight reduction, but showed no change with moderate weight reduction or in those who were weight stable. It is likely that the higher dietary Ca intake during

**Table 3.** Correlations between the changes ( $\Delta$ ) of variables measured.

$\Delta$	Serum $^{206}\text{Pb}$	Weight	Calcium intake	Serum osteocalcin	Serum NTx	Urinary PYD	Urinary DPD
<i>Weight</i>							
R	<b>-0.2387</b>	—	—	—	—	—	—
p	<b>0.042</b>						
<i>Calcium intake</i>							
R	-0.0438	0.0828	—	—	—	—	—
p	0.7132	0.4862					
<i>Serum osteocalcin</i>							
R	0.1726	<b>-0.6548</b>	0.0075	—	—	—	—
p	0.1442	<b>&lt;0.0001</b>	0.9501				
<i>Serum NTx</i>							
R	0.1437	<b>-0.6944</b>	-0.0771	<b>0.5287</b>	—	—	—
p	0.2387	<b>&lt;0.0001</b>	0.5288	<b>&lt;0.0001</b>			
<i>Urinary PYD</i>							
R	<b>0.2968</b>	<b>-0.726</b>	-0.1129	<b>0.575</b>	<b>0.5936</b>	—	—
p	<b>0.0113</b>	<b>&lt;0.0001</b>	0.3452	<b>&lt;0.0001</b>	<b>&lt;0.0001</b>		
<i>Urinary DPD</i>							
R	<b>0.2541</b>	<b>-0.4954</b>	0.0552	<b>0.4886</b>	<b>0.4132</b>	<b>0.749</b>	—
p	<b>0.0313</b>	<b>&lt;0.0001</b>	0.6452	<b>&lt;0.0001</b>	<b>0.0005</b>	<b>&lt;0.0001</b>	
<i>Urinary calcium</i>							
R	-0.1969	<b>0.3546</b>	0.0175	-0.2182	-0.2011	-0.1667	-0.0569
p	0.0974	<b>0.0022</b>	0.8838	0.0656	0.1001	0.1648	0.6376

Abbreviations: DPD, deoxypyridinoline cross-links; NTx, N-telopeptide of type I collagen; Pb, lead; PYD, pyridinoline cross-links.  $n = 73$  (except  $n = 69$  for NTx).

moderate weight reduction in this study prevented an increase in bone resorption that has been found in previous trials, where Ca intake was below 700 mg/day (Ricci et al., 1998). Overall, a greater increase in BPb was directly associated with greater weight reduction and a rise in urinary bone resorption markers. Whether or not the absolute Pb levels vary throughout the period of caloric restriction or if higher values persist after weight stabilizes is likely related to the extent of skeletal mobilization at any given time.

Exposure to Pb over the course of a lifetime results in accumulation of Pb in bones. Thus, older persons are at higher risk of resorptive bone loss and, therefore, higher BPb levels, as also shown in this data set. There may be gender differences in the risk associated with Pb exposure, and whereas men generally have higher blood levels of Pb (Vahter et al., 2006), women typically have more physiological stresses causing more episodes of high bone turnover and potential Pb release into circulation. Dieting without adequate Ca intake and periods of acute and severe caloric restriction are physiological stresses that increase bone turnover and, in turn, may increase BPb.

BPb levels in this overweight and severely obese population were at expected levels for U.S. adults, at 1.5  $\mu\text{g}/\text{dl}$  (Muntner et al., 2005). The absolute increase in BPb levels was only

2.1  $\pm$  3.9  $\mu\text{g}/\text{dl}$  for the women with severe weight loss in this study with a final value of about 4  $\mu\text{g}/\text{dl}$ . Lead exposure at an earlier age has been shown to increase the body Pb burden in humans (Lee et al., 2005) and rats (Han et al., 1997). However, in the current population, significant amounts of early Pb exposure are less probable as these individuals were from a middle-higher socioeconomic status. The National Institute for Occupational Safety and Health (NIOSH) and Center for Disease Control (CDC) suggest that Pb overexposure in the adult is defined as a BPb greater than or equal to 25  $\mu\text{g}/\text{dl}$ . However, sBPb levels as low as 5–9  $\mu\text{g}/\text{dl}$  has been associated with an increased risk of death from all causes, cardiovascular disease, and cancer (Menke et al., 2006; Schober et al., 2006). Others have suggested that patients with metabolic syndrome may have a greater susceptibility for toxicity at lower blood and organ Pb levels (Tsaih et al., 2004; Park et al., 2006). Since metabolic syndrome is a criterion for weight loss surgery, a lower threshold of “normal” blood Pb levels may be relevant to this population. Nevertheless, the low levels of BPb in most of the women (Figure 3) suggest that the advantages of reducing excess weight and symptoms associated with metabolic syndrome in severe obesity, outweigh the risk for Pb toxicity.

In this study, BPb levels were lower in those women with higher Ca intake at baseline measurement. This is not surprising, as previous studies have observed an inverse relationship between BPb levels and Ca intake for women of all ages (Lacasana-Navarro et al., 1996; Weyermann and Brenner, 1998; Lacasana et al., 2000). However, after 6 months of weight loss, Ca intake was no longer associated with BPb levels. It may be that Ca intake cannot suppress the high rate of bone turnover associated with severe caloric restriction. Other high bone turnover conditions, such as pregnancy and lactation, show either a beneficial effect of Ca supplementation to reduce mobilization of skeletal mineral stores (Reid et al., 1993; Prince et al., 1995; Cepollaro et al., 1996; Ricci et al., 1998; Shapses et al., 2001) and BPb levels (Hernandez-Avila et al., 2003; Ettinger et al., 2006) or no effect on BPb levels (Hertz-Picciotto et al., 2000; Gulson et al., 2004, 2006). We found a weak association amongst all women between higher Ca intakes and lower bone resorption (PYD cross-links) and BPb levels during caloric restriction. Hence, it is possible that increased Ca intake had a marginal effect on attenuating BPb during severe weight loss, especially if intake was deficient prior to surgery (i.e., single patient example in Figure 3). This is of particular importance because caloric restriction results in Ca intake that is often in the deficient range (Diawara et al., 2006).

There are some limitations of this study. BPb measurements were only taken at baseline and after 6 months. We do not know whether BPb levels were higher or lower during other weeks of weight loss, or whether they decrease or stabilize once weight loss is discontinued. In addition, this study design does not address how BPb levels would change in individuals who are dieting without consuming adequate Ca (i.e., during moderate weight loss, our subjects were given supplement to ensure that Ca intake was not low), and lower intake in more subjects would be expected to increase both bone turnover and BPb levels. Also, as women in the severe weight loss group were not given Ca supplement, reported intake may have been more variable. Furthermore, our population is all female, and primarily Caucasian from a middle socioeconomic background. Thus, the results of this study may not apply to males or nonwhite ethnic groups, who may have had greater Pb exposure (Vahter et al., 2006) or a differential metabolic response to weight reduction.

In conclusion, we show that severe weight reduction results in a significant increase of BPb levels, which can be only partially explained by the increase in bone turnover. Although the absolute BPb levels remained in the low range, severe weight reduction in individuals with an occupational history or hobbies or folk remedies that expose them to Pb would increase the risk for toxicity. Calcium intake had a marginal effect on attenuating Pb levels during weight loss and very high intakes (i.e., >1500 mg/day) are unlikely to further suppress bone turnover or the rise in BPb, yet other

nutritional or pharmaceutical approaches should be considered for high-risk individuals.

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