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Response: Keeping Abreast of New Science

Sinks and Jackson take strong issue with a recent paper in *EHP* by Gulson et al. (1) on the biokinetics of lead transfer from maternal bone and other body lead stores to nursing infants via human breast milk. I wrote an invited Research Highlights paper (2) that accompanied and discussed the larger context and implications of Gulson et al. While Sinks and Jackson did not include my paper in their letter, their criticisms apply to a number of issues addressed in my article.

Sinks and Jackson would have us believe Gulson et al. (1) were guilty of a public health heresy when the latter noted that there may be potential risks for nursing infants if lead intakes via breast milk are elevated because of elevated long-term maternal lead exposures. My quantitative lead exposure risk calculations for nursing infants in Table 1 make it clear that the potential impact of maternal lead burdens for nursing infants across a range of maternal blood lead (BPb) values is not a trivial matter.

The clearly indicated goals of Gulson et al. (1) were to examine and quantitatively characterize 1) *in vivo* lead movement in nursing mothers, specifically bone lead resorption during lactation and nursing, and 2) the toxicokinetic interplay between endogenous (bone) and exogenous (diet) lead in the bodies of these mothers as they relate to transport of maternal lead to breast milk and then to nursing infants. Their findings document that bone lead releases can contribute significantly to breast milk lead and ultimately to infant lead intake in terms of lead source fractional input. The breast milk study was the latest in a published peer-reviewed series by Gulson et al. that used the method of stable lead isotopic ratio analysis to quantify the contribution of bone lead to BPb and lead in other metabolic compartments, and the temporal character of such inputs.

The findings revealed by Gulson et al., when examined with the many studies of breast milk lead levels in lactating and nursing women, indicate that the toxicokinetic parameters governing lead transfer at low concentrations of BPb to breast milk apply to other cases where there were or are high maternal lead exposures. This especially applies to the ratio of breast milk lead to BPb

concentrations, which appears to increase at higher maternal BPb levels.

Neither the Gulson et al. paper nor my perspective article engaged in undue speculation about risks to the early infant from lead exposures arising from quite elevated breast milk lead concentrations. A comparative analysis of the many studies documenting the quantitative ratios between maternal BPb and associated breast milk lead levels readily shows that 1) as BPb increases, not only does the amount of milk lead increase but the fractional distribution may also increase; and 2) at high maternal lead exposures sufficient to produce high maternal BPb levels, mothers will have breast milk lead that may be problematic for their infants' lead exposures.

Sinks and Jackson take Gulson et al. to task for suggesting screening of nursing mothers, particularly those suspected of past or present high lead exposures. This is a peculiar criticism. That lead will enter breast milk from maternal body lead stores in proportion to the lead exposures in nursing mothers is far from new information. New data of Gulson et al. that show a significant fraction of maternal lead released into breast milk would be derived from very high bone lead levels following maternal chronic high lead exposures merely add a transgenerational dimension to established phenomena. They permit one to conclude that such maternal exposures should be monitored. This is the only way to identify the extent of lead releases to breast milk and ultimately to infants. The suggestion is hardly inappropriate.

Sinks and Jackson cite a 1997 report from the government's Health Resources and Services Administration's (HRSA's) National Center for Education in Maternal and Child Health on the medical benefits and contraindications for infant breast milk feeding. The report was authored by an authority on the topic, Ruth A. Lawrence (3). Lawrence's report says clearly that in the case of likely elevated lead exposures, it is advisable to not only screen children (to presumably include nursing infants) but to screen mothers as well.

Sinks and Jackson state that Lawrence's report (3) identified a maternal BPb level of 40 $\mu\text{g}/\text{dl}$ as the upper limit of safe in terms of the amount of lead entering breast milk and amounts of lead ingested by nursing infants. However, the only citation in Lawrence's report used as the basis for the ceiling figure of 40 $\mu\text{g}/\text{dl}$ is a summary 1994 article in the Centers for Disease Control and Prevention's (CDC's) *Morbidity and Mortality Weekly Report* (MMWR) on preliminary Phase 1 National Health and Nutrition Examination Survey (NHANES) III data (4). This MMWR article, however, contains no discussion of lead in breast milk and provides no evidence for selection of any particular infant breast-feeding

safety limit in terms of maternal BPb. In particular, it cannot be used to justify 40 $\mu\text{g}/\text{dl}$ as the upper limit of a safe maternal BPb for nursing mothers. It is also clear that Lawrence (3) is not comfortable with the use of a maternal BPb as high as 40 $\mu\text{g}/\text{dl}$. As noted, Lawrence recommended testing nursing infants for lead exposure even if maternal BPb concentrations are below 40 $\mu\text{g}/\text{dl}$ and to do environmental lead assessments if maternal BPb is above 10 $\mu\text{g}/\text{dl}$.

Lawrence (3) also implies that a breast milk lead level is acceptable if such levels do not materially add to infant lead burdens. Specifically, not only would no net accumulation occur if infant lead intake is less than 5 $\mu\text{g}/\text{day}$, but infant lead burdens acquired *in utero* would begin to show net excretion (negative lead balance) at such low lead intakes.

Use of the high and obsolete maternal BPb value of 40 $\mu\text{g}/\text{dl}$ as the upper limit for producing safe milk lead content, even if it were somehow still relevant, raises the obvious question of what breast milk lead level would be associated with this maternal BPb guideline. Lawrence (3) states that breast milk lead content can typically range up to 15–20% of the maternal BPb level. This is a range consistent with a number of breast milk lead studies in which BPb levels were elevated. Selection of 15% as the ratio results in a breast milk level of 60 $\mu\text{g}/\text{l}$ (6 $\mu\text{g}/\text{dl}$) for a maternal BPb of 40 $\mu\text{g}/\text{dl}$.

I am not aware of any published toxicokinetic analysis or any other credible quantitative risk assessment of breast milk lead intakes by nursing infants that would validate a maternal BPb level of 40 $\mu\text{g}/\text{dl}$ as the upper limit of safe with regard to resulting lead levels in breast milk and infant BPb levels. I have carried out an analysis of the 40 $\mu\text{g}/\text{dl}$ BPb value, as part of a series of selected maternal BPb levels, in terms of resulting infant BPb levels. The results are in Table 1.

Table 1 presents modeled infant exposures using the EPA's Integrated Exposure-Uptake Biokinetic (IEUBK) computer model for this purpose. This well-validated model is in routine use by risk assessors (5). The modeling results provide both geometric mean (GM) BPb concentrations and the percentages of these nursing infants, 0–6 months of age, who would exceed the CDC action level of 10 $\mu\text{g}/\text{dl}$ and exceed the medical intervention, Class III CDC risk level of 20 $\mu\text{g}/\text{dl}$. Infant BPb mean levels in Table 1 are model-estimated from postnatal milk lead intakes plus body lead at birth from prenatal maternal exposures.

Table 1 shows that the only "safe" level, in terms of the fraction of infants with >20 $\mu\text{g}/\text{dl}$, would be maternal BPb of 15 $\mu\text{g}/\text{dl}$ if no more than 5% of infants are to exceed the 20- $\mu\text{g}/\text{dl}$ figure. If the risk management restriction is no more than 1% to exceed this

value, a maternal BPb value of 10 µg/dl, as seen in Table 1, should not be exceeded. If no more than 5% of breast-feeding infants are to exceed the 10 µg/dl action level, then a maternal BPb <10 µg/dl is required.

A sensitivity analysis using various IEUBK modeling runs shows that the infant body lead burden at birth, from *in utero* accumulation via maternal lead exposures, is mainly expressed through estimated BPb values in the first 6 months of infant life, as compared to the second 6 months of infant life or as compared to exposure integrated over the entire first year of infant life. This is to be expected, given the relatively high biokinetic mobility of lead in the very young. However, it is precisely in the first 6 months of infant life that breast-feeding is done. Therefore, both breast milk lead and prior infant body lead burden are significant sources of lead in breast-feeding infants of mothers with elevated lead exposures. In essence, the only maternal BPb level that is in fact "safe" in terms of CDC Class III elevated infant BPb figures also approximates the CDC infant BPb action level of 10 µg/dl. In terms of the child action level of 10 µg/dl, a maternal BPb <10 µg/dl appears prudent.

The 1991 CDC statement on childhood lead poisoning (6) identified a BPb level of 10 µg/dl as being the body lead threshold associated with the earliest toxic effects in infants and toddlers. The CDC document also accepted the risk assessment premise that there is no known threshold for lead's subtle toxicity.

Sinks and Jackson argue that the most recent NHANES III, 1991–1994, indicates that there are no women in the United States who are likely to be nursing their infants and who have BPb values anywhere close to the 40 µg/dl Sinks and Jackson claimed as permissible for nursing mothers. They cite some actual numbers noted in the NHANES III data tapes (7). Such prevalence data are aggregated cluster sample depictions at a single time point of the U.S. population lead exposure picture, stratified by national socioeconomic

and demographic strata. One cannot legitimately disaggregate such national depictions or "snapshots" to generate comparisons for individual community prevalences or to use actual BPb values contained in any particular statistical sampling cell in the aggregation process. Such limits are discussed in, among other things, the Executive Summary of the 1988 report to the U.S. Congress on childhood lead poisoning (8) by the Agency for Toxic Substances and Disease Registry.

Sinks and Jackson offer the simplistic and incorrect argument that if women in the United States were nursing their infants and had elevated BPbs from workplace exposures, they would be readily and reliably detected by Occupational Safety and Health Administration (OSHA)-required exposure and medical surveillance. Many small operations are either exempt from OSHA requirements because of size or are rarely if ever inspected because of severe resource constraints on federal or various state OSHA agencies. Such assessments similarly would not detect the women who potentially have elevated BPb values owing to environmental, not occupational, lead exposures. A much better approach, regardless of sources of high maternal exposure, would be the approach endorsed by Lawrence (3): maternal/infant screening.

The letter by Sinks and Jackson may be seen by some as another example of an overall CDC retreat from lead as a persisting child health issue. Needleman (9) noted an overall backpedaling in efforts and decline in momentum to finally address the lead issue in a meaningful way by the federal government. All this raises a legitimate question among scientists and clinicians interested in lead: Is lead still considered to be a child health risk issue at the CDC or elsewhere in the federal government?

The actual content of new research should be understood before wholesale attacks on such research are launched. This is especially the case where complex research designs and equally complex results are at work. In those cases where breast milk does not contain worrisome lead concentrations

from high maternal lead exposures, per Table 1, I agree with the Sinks and Jackson comment that "breast is best."

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Response to Sinks and Jackson

We appreciate Sinks' and Jackson's interest in our article on lead in breast milk and would like to reinforce and clarify a couple of points. Paul Mushak has responded comprehensively to their letter, and we are in complete agreement with his response.

We agree wholeheartedly that "breast is best," and our low concentrations of lead in breast milk confirm this. Our abstract (1) was quite emphatic that

Breast-fed infants are only at risk if the mother is exposed to high concentrations of contaminants either from endogenous sources such as the skeleton or exogenous sources.

Sinks and Jackson are dismissive of the use of lead isotopic ratios as not being "meaningful in establishing risk for lead poisoning." Perhaps this is true in the strict sense of risk assessment, but lead isotopic ratios are the only realistic method of determining the source of a mother's lead burden.

Table 1. Predicted blood lead (BPb) levels in breast-feeding infants at various maternal BPb levels^a

| Maternal nursing BPb (µg/dl) ^b | Infant Pb intake (µg/day) ^c | GM infant BPb (µg/dl) ^d | % >10 µg/dl ^e | % >20 µg/dl ^f |
|---|--|------------------------------------|--------------------------|--------------------------|
| 40 | 48 | 19.4 | 90.7 | 45.1 |
| 30 | 36 | 15.4 | 78.4 | 26.9 |
| 20 | 24 | 11.3 | 58.3 | 10.6 |
| 15 | 18 | 9.1 | 40.4 | 4.4 |
| 10 | 12 | 6.9 | 19.8 | 1.0 |

GM, geometric mean.

^aEPA's Integrated Exposure-Uptake Biokinetic Model, Version 0.99d; input parameters were milk Pb uptake = 50%; 0 ml tap water; milk Pb = 100% diet + fluid Pb; model default dust/soil inputs for 0–12-month-old infants.

^bBreast milk feeding period, 0–6 months of age; maternal BPb levels are present at birth through 6 months.

^cInfant Pb intake/day = 0.15 × maternal BPb (µg/dl) × 8 dl milk/day.

^dGeometric standard deviation = 1.6; GM infant BPb and percentages exceeding cutoffs obtained from graphic outputs expressed as probability density function histograms versus infant BPb and using age band "A" (0–6 months of age).

^eCDC action level of ≥10 µg/dl.

^fCDC Class III, medical intervention level of ≥20 µg/dl.