Research conducted in recent years has increased public health concern about the toxicity of lead at low dose and has supported a reappraisal of the levels of lead exposure that may be safely tolerated in the workplace. In this article, which appears as part of a mini-monograph on adult lead exposure, we summarize a body of published literature that establishes the potential for hypertension, effects on renal function, cognitive dysfunction, and adverse female reproductive outcome in adults with whole-blood lead concentrations < 40 µg/dL. Based on this literature, and our collective experience in evaluating lead-exposed adults, we recommend that individuals be removed from occupational lead exposure if a single blood lead concentration exceeds 30 µg/dL or if two successive blood lead concentrations measured over a 4-week interval are ≥ 20 µg/dL. Removal of individuals from lead exposure should be considered to avoid long-term risk to health if exposure control measures over an extended period do not decrease blood lead concentrations to < 10 µg/dL or if selected medical conditions exist that increase the risk of continued exposure. Recommended medical surveillance for all lead-exposed workers should include quarterly blood lead measurements for individuals with blood lead concentrations between 10 and 19 µg/dL, and semiannual blood lead measurements when sustained blood lead concentrations are < 10 µg/dL. It is advisable for pregnant women to avoid occupational or avocational lead exposure that would result in blood lead concentrations > 5 µg/dL. Chelation may have an adjunctive role in the medical management of highly exposed adults with symptomatic lead intoxication but is not recommended for asymptomatic individuals with low blood lead concentrations. Key words: adult lead exposure, blood lead, chelation, medical management, medical surveillance, pregnancy.

Table 1 is a summary of the adverse health risks associated with different blood lead concentrations and presents corresponding medical management recommendations that range from discussion of risks and issues. In deriving the recommendations in this article, we took note of a body of literature that establishes the potential for adverse health effects at blood lead concentrations or exposure levels permissible under current workplace regulations established in the 1970s by the U.S. Occupational Safety and Health Administration (OSHA). These regulations generally require removal from lead exposure when whole-blood lead concentrations exceed 50 or 60 µg/dL. These values are considerably above blood lead concentrations of the general population of the United States, which had a geometric mean of 12.8 µg/dL in the late 1970s (National Center for Health Statistics 1984), and a recent value of 1.45 µg/dL [U.S. Centers for Disease Control and Prevention (CDC) 2005].

In setting forth our perspective on the recommended medical management of adult lead exposure, the narrative of this article focuses on four categories of health effects—hypertension, decrement in renal function, cognitive dysfunction, and adverse reproductive outcome—that have been the subject of much recent research. The discussion of these end points highlights those studies, that by virtue of their design and scope, were particularly influential in establishing the authors’ concerns regarding the potential for adverse health effects at low to moderate levels of lead exposure in adults. Collectively, these effects support the preventive medical management strategies that are recommended in the tables. A review of the extensive literature on the health effects of lead is beyond the scope of this article, but the reader is referred to reviews on the cardiovascular and cognitive impacts of lead on adults that appear elsewhere in this mini-monograph (Navas-Acien et al. 2007; Shih et al. 2007), as well as a review on recent lead literature prepared by the U.S. Environmental Protection Agency (EPA) for its Air Quality Criteria for Lead (U.S. EPA 2006).

This article is part of the mini-monograph “Lead Exposure and Health Effects in Adults: Evidence, Management, and Implications for Policy.”

Address correspondence to M. Kosnett, 1630 Welton St., Ste. 300, Denver, CO 80202 USA. Telephone: (303) 571-5778. Fax: (303) 571-5820. E-mail: Michael.Kosnett@uchsc.edu

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reduction of lead exposure at low levels to removal from lead exposure accompanied by probable chelation therapy at the highest levels. The designation of risks as either “short-term” or “long-term,” depending on whether the risks are associated with exposure lasting less than or more than 1 year, reflects a qualitative understanding of the duration of lead exposure that may be required to elicit certain adverse health effects of lead. For some of the long-term risks, such as hypertension, research employing noninvasive K-shell X-ray fluorescence measurement of lead in bone, a biomarker of long-term cumulative exposure, suggests that several years of sustained elevations in blood lead may be necessary for a significant risk to emerge. The use of 1 year as a cut-point in the table is not intended to represent a sharp division, in terms of cumulative dose, between what might constitute a short-term versus a long-term risk nor does it imply that a significant long-term risk begins to exist as soon as 1 year is surpassed. Blood lead, a measure of the amount of lead circulating in the tissues, reflects both recent exogenous exposure as well as endogenous redistribution of lead stored in bone.

The categorization of risks in Table 1 by discrete intervals of blood lead concentration is a qualitative assessment. In clinical practice, substantial interindividual variability in the susceptibility to symptomatic adverse effects of lead is commonly observed. Factors that might influence the risk of lead toxicity in adults include preexisting disease affecting relevant target organs (e.g., hypertension, renal disease, or neurologic dysfunction), nutritional deficiencies that modify the absorption or distribution of lead (e.g., low dietary calcium or iron deficiency), advanced age, and genetic susceptibility. Although recent studies suggest that polymorphisms in specific genes may modify the toxicokinetics and renal effects of lead (Thépée et al. 2004; Weaver et al. 2006; Wu et al. 2003), research findings at present are insufficient to conclusively identify genotypes that confer increased risk.

Table 1. Health-based management recommendations for lead-exposed adults.

| Blood lead level (µg/dL) | Short-term risks (lead exposure < 1 year) | Long-term risks (lead exposure ≥ 1 year) | Management |
|--------------------------|-------------------------------------------|------------------------------------------|------------|
| < 5                      | None documented                           | None indicated                           |            |
| 5–9                      | Possible spontaneous abortion             | Possible spontaneous abortion             |            |
|                          | Possible postnatal developmental delay    | Possible postnatal developmental delay    |            |
|                          | Possible postnatal developmental delay    | Possible lead exposure for women who are or may become pregnant |
| 10–19                    | Possible spontaneous abortion             | Reduced birth weight                     |            |
|                          | Possible postnatal developmental delay    | Hypertension and kidney dysfunction       |            |
|                          | Reduced birth weight                     | Possible subclinical neurocognitive deficits |
|                          | Hypertension and kidney dysfunction       | As above for BLL 5–9 µg/dL, plus:        |
|                          | Possible subclinical neurocognitive deficits | Decrease lead exposure                   |
|                          | Spontaneous abortion                     | Consider removal from lead exposure to avoid long-term risks if exposure control over an extended period does not decrease BLL < 10 µg/dL, or if medical condition present that increases risk with continued exposure³ |
| 20–29                    | Possible spontaneous abortion             | Reduced birth weight                     |            |
|                          | Possible postnatal developmental delay    | Reduced birth weight                     |            |
|                          | Reduced birth weight                     | Possible subclinical neurocognitive deficits |
|                          | Hypertension and kidney dysfunction       | Remove from lead exposure                |
|                          | Possible subclinical neurocognitive deficits | remains ≥ 20 µg/dL                       |
| 30–39                    | Spontaneous abortion                      | Spontaneous abortion                     |            |
|                          | Possible postnatal developmental delay    | Reduced birth weight                     |            |
|                          | Reduced birth weight                      | Possible postnatal developmental delay    |
|                          | Hypertension and kidney dysfunction       | Possible subclinical neurocognitive deficits |
|                          | Possible subclinical neurocognitive deficits | Remove from lead exposure                |
| 40–79                    | Spontaneous abortion                      | Spontaneous abortion                     |            |
|                          | Reduced birth weight                      | Reduced birth weight                     |            |
|                          | Possible postnatal developmental delay    | Possible postnatal developmental delay    |
|                          | Nonspecific symptoms³                     | Nonspecific symptoms³                     |            |
|                          | Neurocognitive deficits                   | Hypertension                             |
|                          | Sperm abnormalities                       | Kidney dysfunction/nephropathy            |
|                          | Possible neurocognitive deficits          | Subclinical peripheral neuropathy         |
|                          | Anemia                                    | Neurocognitive deficits                   |
|                          | Colic                                     | Spasm abnormalities                      |
|                          | Possible gout                             | Remove from lead exposure                |
|                          | Possible hypertension and kidney dysfunction | Refer for prompt medical evaluation       |
|                          | Possible subclinical neurocognitive deficits | Consider chelation therapy for BLL > 50 µg/dL with significant symptoms or signs of lead toxicity |
| ≥ 80                     | Spontaneous abortion                      | Spontaneous abortion                     |            |
|                          | Reduced birth weight                      | Reduced birth weight                     |            |
|                          | Possible postnatal developmental delay    | Possible postnatal developmental delay    |
|                          | Nonspecific symptoms³                     | Nonspecific symptoms³                     |            |
|                          | Neurocognitive deficits                   | Hypertension                             |
|                          | Sperm abnormalities                       | Kidney dysfunction/nephropathy            |
|                          | Anemia                                    | Neurocognitive deficits                   |
|                          | Colic                                     | Spasm abnormalities                      |
|                          | Gout                                      | Remove from lead exposure                |

BLL, blood lead level.

*Medical conditions that may increase the risk of continued exposure include chronic renal dysfunction (serum creatinine > 1.5 mg/dL for men and > 1.3 mg/dL for women, or proteinuria), hypertension, neurologic disorders, and cognitive dysfunction. *Nonspecific symptoms may include headache, fatigue, sleep disturbance, anorexia, constipation, arthralgia, myalgia, and decreased libido.
Health Effects at Low Dose

Hypertension. Animal investigations support a pressor effect of lead at low dose (Fine et al. 1988; Gonick et al. 1997; Vaziri 2002). Epidemiologic investigations conducted in large general population samples (e.g., Harlan 1988; Nash et al. 2003; Pocock et al. 1988; Schwartz 1988) suggest lead may elevate blood pressure in adults at blood lead concentrations < 20 µg/dL. In some human studies of the link between blood lead and blood pressure, the relationship appeared to be influenced by subjects’ sex or race (e.g., Den Hond et al. 2002; Staessen et al. 1996; Vupputuri et al. 2003). Three meta-analyses of studies examining the relationship between blood lead and blood pressure found relatively consistent effects of blood lead on blood pressure. The studies showed statistically significant coefficients for a 2-fold increase in blood lead of 1.0 mmHg (Nawrot et al. 2002; Staessen et al. 1994) or 1.25 mmHg (Schwartz 1995) for systolic blood pressure, and 0.6 mmHg for diastolic blood pressure (Nawrot et al. 2002; Staessen et al. 1994). The study populations analyzed in these meta-analyses included many with blood lead concentrations < 20 µg/dL.

Further support for the impact of low-level lead exposure on blood pressure has emerged from studies employing K-shell X-ray fluorescence measurement of lead in bone, a biomarker of long-term cumulative lead exposure. In two major studies drawn from samples of the general population, bone lead concentrations were a significant predictor of cardiovascular mortality. Because of their size and design, studies derived from the National Health and Nutrition Examination Surveys (NHANES) are particularly notable. A 16-year longitudinal analysis of the general population cohort studied between 1976 and 1980 as part of NHANES II found that blood lead concentrations of 20–29 µg/dL at baseline were associated with 39% increased mortality from circulatory system disease compared with subjects with blood lead < 10 µg/dL [relative risk (RR) 1.39; 95% CI, 1.01–1.91] (Lustberg and Silbergeld 2002).

Two studies recently examined the longitudinal relationship between blood lead concentration and cardiovascular mortality among participants in NHANES III. In a 12-year longitudinal study of participants in NHANES III, ≥ 40 years of age (n = 9,757), the subgroup with blood lead concentration ≥ 10 µg/dL (median, 11.8) had a relative risk of cardiovascular mortality of 1.59 (95% CI, 1.28–1.98) compared with subjects with blood lead < 5 µg/dL (Schober et al. 2006). In a 12-year longitudinal analysis of subjects ≥ 17 years of age (n = 13,946), the relative risk for cardiovascular mortality was 1.53 (95% CI, 1.21–1.94), comparing a blood lead of 4.92 µg/dL (80th percentile of the distribution) with a blood lead of 1.46 µg/dL (20th percentile of the distribution) (Menke et al. 2006).

Renal effects. Renal injury that appears after acute high-dose lead exposure may include reversible deficits in proximal tubular reabsorption and preternal azotemia induced by renal vasoconstriction and/or volume depletion (Coyle et al. 200; Wedeen et al. 1979). In a minority of exposed individuals, years of chronic, high-dose lead exposure may result in chronic lead nephropathy, a slowly progressive interstitial fibrosis characterized by scant proteinuria (Lilis et al. 1968). Epidemiologic investigations of renal function in workers with lower levels of chronic lead exposure have yielded variable findings. For example, in a cohort of approximately 800 current and former lead workers with mean blood lead of 32 ± 15 µg/dL, there was no significant linear relationship between blood lead concentration and two measures of renal function, serum creatinine and creatinine clearance (Weaver et al. 2003). There was an interaction between age and tibia lead concentration, a biomarker of cumulative lead exposure, on these same biomarkers, resulting in a trend toward worse renal function with increasing bone lead in the oldest tertile of workers (> 46 years of age) but improved renal function with increasing bone lead in the youngest workers (≤ 36 years of age). The authors suggested that lead-induced hyperfiltration, a finding noted in other studies, might presage the eventual development of lead-induced renal insufficiency. Both blood lead and tibia lead were correlated with increased urinary N-acetyl-p-D-glucosaminidase (NAG), a biomarker of early biological effect on the renal tubule, but in an analysis of a smaller subset of the lead workers (n = 190) that controlled for the relatively low levels of urinary cadmium (1.1 ± 0.78 µg/g creatinine), only the relationship with tibia lead and NAG remained significant (Weaver et al. 2003).

Among a cohort of 70 active lead workers with a median blood lead concentration of 32 µg/dL (range, 5–47), there were modest correlations between blood lead and urinary β-2-microglobulin (r = 0.27; p = 0.02), and between cumulative blood lead index and NAG (r = 0.25; p = 0.04) (Gerhardsson et al. 1992).

Several studies conducted in general population samples have reported an association between blood lead concentration and common biomarkers of renal function (serum creatinine and creatinine clearance). In a cross-sectional investigation of a subcohort of middle-aged to elderly men enrolled in the Normative Aging Study (n = 744), there was a negative correlation between blood lead (mean, 8.1 ± 3.9 µg/dL; range, 4.0–26.9 µg/dL) and measured creatinine clearance, after natural log transformation of both variables and adjustment for other covariates (Payton et al. 1994). Among an adult population that included subjects with environmental cadmium exposure (n = 965 men (geometric mean blood lead, 11.4 µg/dL; range, 2.3–72.5 µg/dL); n = 1,016 women (geometric mean blood lead, 7.5 µg/dL; range, 1.7–60.3 µg/dL)), log-transformed blood lead concentration was inversely correlated with measured creatinine clearance (Staessen et al. 1992). In a population-based study of Swedish women 50–59 years of age (n = 820), low levels of blood lead (mean, 2.2 µg/dL; 5th–95th percentiles, 1.1–4.6 µg/dL) were inversely correlated with creatinine clearance and glomerular filtration rate, after adjusting for age, body mass index, urinary or blood cadmium, hypertension, diabetes, and regular use.
of nonsteroidal anti-inflammatory drug (NSAID) medication (Akesson et al. 2005).

Individuals with other risk factors for renal disease, notably hypertension and diabetes, may be more susceptible to an adverse impact of low-level lead exposure on renal function. Among adults participating in NHANES III \( (n = 15,211) \), blood lead was a risk factor for elevated serum creatinine \( (\text{defined as a 99th percentile of the analyte’s race and sex specific distributions, generally } > 1.2–1.5 \text{ mg/dL}) \) and “chronic kidney disease” \( (\text{defined as an estimated glomerular filtration rate } < 60 \text{ mL/min}) only among subjects with hypertension \( (n = 4813) \) (Muntener et al. 2003). Compared with hypertensives in the lowest quartile of blood lead \( (\text{range, 0.7–2.4 } \mu \text{g/dL}) \), hypertensive subjects in the next highest quartile of blood lead \( (\text{range, 2.5–3.8 } \mu \text{g/dL}) \) had a covariate-adjusted OR for elevated serum creatinine \( (1.47 \text{ (95\% CI, 1.03–2.10)} \) and for chronic kidney disease \( (1.44 \text{ (95\% CI, 1.00–2.09)} \). At the next highest quartile of blood lead \( (\text{range, 3.9–5.9 } \mu \text{g/dL}) \), the covariate-adjusted OR for elevated serum creatinine \( = 1.80 \text{ (95\% CI, 1.34–2.42)} \), and for chronic kidney disease \( = 1.85 \text{ (95\% CI, 1.32–2.59)} \). In a subcohort of middle-aged to elderly men participating in the Normative Aging Study \( (n = 427) \), blood lead \( (4.5 \pm 2.5 \mu \text{g/dL}) \), multiple regression analysis revealed that log-transformed blood lead was positively correlated with serum creatinine in hypertensive but not normotensive subjects (Tsaih et al. 2004). In a longitudinal study of this cohort over a mean of 6 years, an interaction between lead and diabetes yielded a positive association between baseline blood lead concentration and change in serum creatinine that was strongest in diabetic subjects (Tsaih et al. 2004). An interaction with diabetes was also present in the association of tibial lead concentration with longitudinal change in serum creatinine (Tsaih et al. 2004). Although these general population studies are consistent with an adverse effect of lead exposure on renal function at notably low levels, the extent to which diminished renal function may itself result in increased body lead burden has not been fully elucidated.

**Cognitive dysfunction.** A few studies examining relatively small numbers of workers \( (n = 100) \) with blood lead concentrations ranging approximately 20–40 \( \mu \text{g/dL} \) have associated lead exposure with substential decrements in selective domains of neurocognitive function \( (\text{Barth et al. 2002; Hänninen et al. 1998; Muntener et al. 1984; Stolley 1996}). Among a large cohort of current and former inorganic lead workers studied in Korea, a cross-sectional analysis \( (n = 803 \text{ workers}) \) (Schwartz et al. 2001) and a 3-year longitudinal analysis \( (n = 576 \text{ workers}) \) (Schwartz et al. 2005) found that blood lead concentrations across the approximate range of 20–50 \( \mu \text{g/dL} \) were associated with subclinical neurocognitive deficits. Among a small population of former lead workers \( (n = 48) \) and age-matched controls with similar blood lead concentrations \( (\text{approximately } 5 \mu \text{g/dL in both groups; range, 1.6–14.5 } \mu \text{g/dL; mean age, 39.8 years}) \), increases in current blood lead concentration within the entire study population were correlated with poorer performance on several tests of neurocognitive function but on only one measure was cumulative lead exposure \( (\text{measured in the workers}) \) associated with poorer performance (Winker et al. 2005).

In the population-based sample of adults 20–59 years of age participating in the NHANES III study \( (n = 4937) \), there was no relationship between blood lead concentration \( (\text{geometric mean, 2.51 } \mu \text{g/dL}) \) and covariate-adjusted performance on neurocognitive function \( (Krieg et al. 2005) \). However, significant associations have emerged in some studies of older adults with slightly higher blood lead concentrations. In a rural subset of elderly women \( (\text{mean age, 71.1 } \pm 4.7 \text{ years; } n = 325) \) with background, community lead exposure \( (\text{geometric mean blood lead concentration, 4.8 } \mu \text{g/dL; range, 1–21 } \mu \text{g/dL}) \), certain measures of neuropsychologic function \( (\text{Trailmaking part B and Digit Symbol test}) \) were performed more poorly by women in the upper 15th percentile of blood lead \( (\text{blood lead } \geq 8 \mu \text{g/dL; } n = 38; \text{Muldoon et al. 1996}) \). However, in the slightly younger subset of elderly women who resided in an urban area \( (\text{mean age, 69.4 } \pm 3.8 \text{ years; } n = 205) \), no relationship between blood lead \( (\text{geometric mean, 5.4 } \mu \text{g/dL}) \) and neuropsychologic performance was discernible \( (\text{Muldoon et al. 1996}) \). In a general population sample of middle-aged to elderly men \( (n = 141; \text{mean age, 66.8 } \pm 6.8 \text{ years}) \) with a mean blood lead concentration \( (3.5 \pm 3.5 \mu \text{g/dL}) \), examined as part of the Normative Aging Study, increased blood lead concentration was associated with poorer performance on neuropsychologic assessment of memory, verbal ability, and mental processing speed \( (\text{Payton et al. 1998}) \). In a larger subset of men \( (n = 736; \text{mean age, 68.2 } \pm 6.9 \text{ years}) \) from the Normative Aging Study assessed with the Mini-Mental Status Examination (MMSE), the OR for having a test score associated with an increased risk of dementia \( = 3.4 \text{ (95\% CI, 1.6–7.2)} \) comparing the mean blood lead of the highest quartile \( (\text{mean, 8.9 } \mu \text{g/dL}) \) to that of the lowest quartile \( (\text{mean, 2.5 } \mu \text{g/dL}) \) (Wright et al. 2003). There was a positive interaction between age and blood lead, which is consistent with a lead-associated acceleration in age-related neurodegeneration.

As reviewed in an accompanying article in this mini-monograph \( (Shih et al. 2007), there is evidence that at low levels of lead exposure, biomarkers of cumulative lead exposure, such as lead in bone, may be associated with an adverse impact on neurocognitive function that is not reflected by measurement of lead in blood. Among subjects from the Normative Aging Study \( (n = 466; \text{mean age, 67.4 } \pm 6.6 \text{ years}) \) examined for longitudinal change in MMSE score over an average of \( 3.5 \pm 1.1 \text{ years}, higher patella bone lead concentrations, a biomarker of cumulative lead exposure, predicted a steeper decline in performance \( (Weisskopf et al. 2004) \). By comparison, baseline blood lead concentration \( (\text{median, 4 } \mu \text{g/dL; interquartile range } = 3, 5) \) did not predict change in MMSE score. In a longitudinal analysis of performance on a battery of cognitive tests in a subset of the Normative Aging Study, bone lead measurements were predictive of worsening performance over time on tests of visuospatial/visuomotor ability \( (Weisskopf et al. 2007) \). In a cross-sectional analysis of 985 community dwelling residents 50–70 years of age, increasing tibia bone lead concentrations were significantly associated with decrements in cognitive function, whereas an impact of blood lead \( (\text{mean, 3.46 } \pm 2.23 \mu \text{g/dL}) \) was not apparent \( (Shih et al. 2006) \).

**Reproductive outcome in women.** Adverse effects on reproductive outcome constitute a special risk of lead exposure to women of reproductive age. A nested case–control study examined the association of blood lead concentration with spontaneous abortion in a cohort of 668 pregnant women seeking prenatal care in Mexico City \( (Borja-Aburto et al. 1999) \). After matching for maternal age, education, gestational age at study entry, and other covariates, the OR for spontaneous abortion before 21 weeks gestation was 1.13 \( (95\% \text{ CI, 1.01–1.30}) \) for every 1 \( \mu \text{g/dL} \) increase in blood lead across the blood lead range of 1.4–29 \( \mu \text{g/dL} \). Compared with the reference category of < 5 \( \mu \text{g/dL} \), ORs for spontaneous abortion of 2.3, 5.4, and 12.2, respectively \( (p = 0.03) \). Although several earlier studies failed to detect this substantial impact, they may have been subject to methodologic limitations not present in the Mexico City investigation \( (Hertz-Picciotto 2000) \). Several studies have found that lead exposure during pregnancy affects child physical development measured during the neonatal period and early childhood. In an extensively studied cohort of 272 full-term, parturient women from Mexico City with environmental lead exposure common to the region \( (\text{mean maternal blood lead, 8.9 } \pm 4.1 \mu \text{g/dL}) \), mean...
tibia bone lead, 9.8 ± 8.9 µg/g; range, 12–38 µg/g), every increase of 10 µg/g in maternal tibia lead was associated with a 73-g (95% CI, 25–121) decrease in birth weight (Gonzalez-Cossio et al. 1997). The impact of tibia bone lead on birth weight was nonlinear and was most pronounced in mothers with the highest quartile of bone lead (> 15–38 µg/g) where the decrement relative to the lowest quartile was estimated to be 156 g. Primarily in the same cohort, a maternal patella lead concentration > 24.7 µg/g was associated with an OR of 2.35 (95% CI, 1.26–4.40) for a neonate with one category smaller head circumference at birth, assessed as a five-category–ordered variable (Hernandez-Avila et al. 2002). In a different Mexico City cohort, each doubling of maternal blood lead at 36 weeks of pregnancy (geometric mean, 8.1 µg/dL; 25th–75th percentile, 5–12 µg/dL) was associated with a decrease of 0.37 cm (95% CI, 0.57–0.17) in the head circumference of a 6-month-old infant (Rothenberg et al. 1999b).

Prenatal lead exposure assessed by umbilical cord blood lead concentration has been inconsistently associated with an adverse effect on neurobehavioral development in childhood. However, recent studies suggest that mobilization of maternal bone lead during pregnancy may contribute to fetal lead exposure in ways that may be incompletely reflected by the single measurement of umbilical cord whole-blood lead (Chuang et al. 2001; Tellez-Rojo et al. 2004). In a prospective study conducted in Mexico City of 197 mother–infant pairs, a statistically significant adverse effect of umbilical cord blood lead (mean, 6.7 ± 3.4 µg/dL; range, 1.2–21.6 µg/dL) was also accompanied by an independent adverse effect of maternal bone lead burden on the 24-month Mental Development Index (MDI) of the Bayley Scales of Infant Development, which decreased 1.6 points (95% CI, 0.2–3.0) for every 10-µg/g increase in maternal patellar lead (mean, 17.9 ± 15.2 µg/g; range, < 1–76.6 µg/g) (Goma et al. 2002). A prospective study that measured maternal plasma lead and maternal whole-blood lead during pregnancy found that maternal plasma lead during the first trimester was the strongest predictor of infant mental development. The corresponding impact of one SD increase in loge maternal whole blood during the first trimester was a 2.4-point decrease in the 24-month MDI. The logarithmic relationship between maternal plasma and blood lead concentrations and infant MDI indicated that the strongest effects occurred among mothers with the lowest plasma and blood lead concentrations.

Two long-term prospective studies that conducted multiple measurements of maternal blood lead during pregnancy and childhood have identified an adverse impact of low-level prenatal lead exposure on postnatal neurobehavioral development extending beyond infancy. Applying a repeated measures linear regression technique to analysis of age-appropriate IQ test data obtained in 390 children 3–7 years of age, the Yugoslavia Prospective Lead Study found independent adverse effects of both prenatal and postnatal blood lead. After controlling for the pattern of change in postnatal blood lead and other covariates, IQ decreased 1.8 points (95% CI, 1.0–2.6) for every doubling of prenatal blood lead, which was assessed as the average of maternal blood lead at midpregnancy and delivery (mean, 10.2 ± 14.4 µg/dL; n = 390) (Wasserman et al. 2000). The Mexico City Prospective Lead Study used generalized linear mixed models with random intercept and slope to assess the impact on IQ measured at 6–10 years of age of blood lead measurements systematically obtained during weeks 12, 20, 24, and 36 of pregnancy, at delivery, and at multiple points throughout childhood (Schnaas et al. 2006). Geometric mean blood lead during pregnancy was 8.0 µg/dL (range, 1–33 µg/dL; n = 150); from 1 through 5 years it was 9.8 µg/dL (2.8–36.4 µg/dL), and from 6 through 10 years it was 6.2 µg/dL (range, 2.2–18.6 µg/dL). IQ at 6 to 10 years of age, assessed by the Wechsler Intelligence Scale for Children—Revised, decreased significantly only with increasing natural-log third-trimester blood lead, controlling for other blood lead measurements and covariates. Every doubling of third trimester blood lead (geometric mean of maternal blood lead at weeks 28 and 36 = 7.8 µg/dL; 5th–95th percentile: range, 2.5–24.6 µg/dL) was associated with an IQ decrement of 2.7 points (95% CI, 0.9–4.4). Notably, the nonlinear (i.e., log-linear) relationships detected in the Yugoslavia and Mexico City studies indicate that across a maternal blood lead range of 1–30 µg/dL, an increase in blood lead from 1 to 10 µg/dL will account for more than half the IQ decrement.

Two independent cohorts have provided evidence that maternal lead burden during pregnancy may be associated with increased risk of pregnancy hypertension and/or elevated blood pressure during pregnancy. In a retrospective study of 3,210 women during labor and delivery, increasing umbilical cord blood lead levels (mean, 6.9 ± 3.3 µg/dL; range, 0–35 µg/dL) were associated with increased systolic blood pressure during labor (1.0 mmHg for every doubling of blood lead) and increased odds of hypertension (not further defined) recorded any time during pregnancy (OR = 1.3; 95% CI, 1.1–1.5) for every doubling of blood lead (Rabinowitz et al. 1987). A prospective study of third trimester blood lead (geometric mean, 2.3 ± 1.4 µg/dL; range, 0.5–36.5 µg/dL) in 1,188 predominantly Latina immigrants showed that, in the immigrants, every doubling in blood lead was associated with increased third-trimester systolic blood pressure (1.2 mmHg; 95% CI, 0.5–1.9) and diastolic blood pressure (1.0 mmHg; 95% CI, 0.4–1.5) (Rothenberg et al. 1999a). A study of a subset of the same cohort (n = 637) without regard to immigration status found that every 10-µg/g increase in calcaneus (heel) bone lead increased the OR of third trimester pregnancy hypertension (systolic > 90 and/or diastolic > 140 mmHg) by 1.86 (95% CI, 1.04–3.32) (Rothenberg et al. 2002).
on its website (OSHA 2005). Venous blood should be used for biological monitoring of adult lead exposures, except where prohibited by medical or other reasons. Routine measurement of zinc protoporphyrin, a requirement of the OSHA lead standards, is not recommended in Table 2 because it is an insensitive biomarker of lead exposures in individuals with blood lead concentrations < 25 µg/dL (Parsons et al. 1991).

The content of the baseline or preplacement history and physical examination for lead-exposed workers should continue to follow the comprehensive scope set forth in the OSHA lead standard for general industry. Measurement of serum creatinine will identify individuals with chronic renal dysfunction who may be subject to increased health risks from lead exposure. With the potential exception of an annual blood pressure measurement and a brief questionnaire regarding the presence of medical conditions (such as renal insufficiency) that might increase the risk of adverse health effects of lead exposure, medical evaluations for lead-exposed workers should be unnecessary as long as blood lead concentrations are maintained < 20 µg/dL. Annual education of lead workers regarding the nature and control of lead hazards, and ongoing access to health counseling regarding lead-related health risks are recommended as preventive measures.

**Lead Exposure during Pregnancy and Lactation**

As summarized earlier in this article, the recent findings concerning lead-related adverse reproductive outcomes render it advisable for pregnant women to avoid occupational or avocational lead exposure that would result in blood lead concentrations > 5 µg/dL. Calcium supplementation during pregnancy may be especially important for women with past exposure to lead. Calcium decreases bone resorption during pregnancy (Janakiraman et al. 2003) and may minimize release of lead from bone stores and subsequent fetal lead exposure (Goma et al. 2002).

Maternal body lead burden and external lead exposure influence the lead concentration of breast milk (Ettinger et al. 2006; Gulson et al. 1998). The few studies that used ultraclean techniques and mass spectrometry analyses report human breast milk concentrations ranging from 0.6 to 3% of maternal blood lead (Ettinger et al. 2004b; Gulson et al. 1998; Manton et al. 2000; Sowers et al. 2002). Using 1% as a guide, it can be estimated that nursing mothers with a blood lead concentration < 20 µg/dL will have breast milk with a concentration < 2 µg/L, a value that approximates the amount of lead in infant formula (Gulson et al. 2001). A recent randomized clinical trial among Mexican women with mean blood lead concentrations of approximately 9 µg/dL found that calcium supplementation during lactation may reduce the lead concentration of breast milk by 5–10% (Ettinger et al. 2006). Breast feeding should be encouraged for almost all women (Ettinger et al. 2004a; Sanin et al. 2001; Sinks and Jackson 1999), with decisions concerning women with very high lead exposure addressed on an individual basis.

**Medical Treatment of Elevated Blood Lead Concentration and Overt Lead Intoxication**

Removal from all sources of hazardous lead exposure, whether occupational or nonoccupational, constitutes the first and most fundamental step in the treatment of an individual with an elevated blood lead concentration. A careful history that inquires about a broad spectrum of potential lead sources is recommended (Occupational Lead Poisoning Prevention Program 2006). Removal from occupational lead exposure will usually require transfer of the individual out of any environment or task that might be expected to raise the blood lead concentration of a person not using personal protective equipment above background levels (i.e., 5 µg/dL). If there has been a history of an affected individual bringing lead-contaminated shoes, work clothes, or equipment home from the workplace, evaluation of vehicles and the home environment for significant levels of lead-containing dust might be considered (Piacitelli et al. 1995). Although such “take-home” exposure might contribute to further lead exposure of the worker, it ordinarily poses more of a potential risk to young children and pregnant or nursing women who share the worker’s home environment (Hippins et al. 2004; Roscoe et al. 1999).

Medical treatment of individuals with overt lead intoxication involves decontamination, supportive care, and judicious use of chelating agents. Comprehensive discussion of such treatment is beyond the scope of this article but has been reviewed in recent medical toxicology texts (Kosnett 2001, 2005). A variety of chelating agents has been demonstrated to decrease blood lead concentrations and increase urinary lead excretion. A recent double-blind randomized clinical trial of oral chelation in young children with blood lead concentrations ranging from 22 to 44 µg/dL found that the drug succimer lowered blood concentrations transiently but did not improve cognitive function (Dietrich et al. 2004; Rogan et al. 2001). Although anecdotal evidence suggests that chelation has been associated with improvement in symptoms and decreased mortality in patients with lead encephalopathy, controlled clinical trials demonstrating efficacy are lacking. Treatment recommendations are therefore mostly empiric, and decisions regarding the initiation of chelation therapy for lead intoxication have occasionally engendered controversy.

In our experience, adults with blood lead concentrations ≥ 100 µg/dL almost always warrant chelation, as levels of this magnitude are often associated with significant symptoms and may be associated with an incipient risk of encephalopathy or seizures. Occasionally, patients with very high blood lead concentrations may have no overt symptoms. Patients with blood lead concentrations of 80–99 µg/dL, with or without symptoms, can be considered for chelation treatment, as may some symptomatologic individuals with blood lead concentrations of 50–79 µg/dL. These demarcations are imprecise, however, and decisions on chelation should be made on a case-by-case basis after consultation with an

**Table 2. Health-based medical surveillance recommendations for lead-exposed workers.**

| Category of exposure | Recommendations |
|----------------------|-----------------|
| All lead-exposed workers* | Baseline or preplacement medical history and physical examination, baseline BLL, serum creatinine |
| BLL (µg/dL) | |
| < 10 | BLL every month for first 3 months of placement, or upon change in task to higher exposure, then BLL every 6 months |
| | If BLL increases ≥ 5 µg/dL, evaluate exposure and protective measures. |
| | Increase monitoring if indicated |
| | See Table 1 for pregnancy concerns |
| 10–19 | As above for BLL < 10 µg/dL, plus: |
| | BLL every 3 months |
| | Evaluate exposure, engineering controls, and work practices |
| | Consider removal (see Table 1) |
| | Revert to BLL every 6 months after 3 BLLs < 10 µg/dL |
| | Remove from exposure if repeat BLL measured in 4 weeks remains ≥ 20 µg/dL, or if first BLL ≥ 20 µg/dL (see Table 1) |
| | Monthly BLL testing |
| | Consider return to lead work after 2 BLLs < 15 µg/dL, a month apart, then monitor as above |

BLL, blood lead level. *Lead-exposed means handling or disturbing materials with a significant lead content in a manner that could reasonably be expected to cause potentially harmful exposure through inhalation or ingestion.
10–19 Discuss health risks. Decrease exposure. Monitor BLL < 5 No action needed

≥20–29 Remove from exposure if repeat BLL in 4 weeks remains ≥ 5–9 Discuss health risks

Blood lead level (µg/dL) Management recommendations and requirements* for adults

< 5 No action needed

5–9 Discuss health risks

Reduce exposure for pregnancy

10–19 Discuss health risks. Decrease exposure. Monitor BLL

Remove from exposure for pregnancy, certain medical conditions, long-term risks

20–29 Remove from exposure if repeat BLL in 4 weeks remains ≥ 20 µg/dL

30–79 Remove from exposure. Prompt medical evaluation and consultation advised for BLL > 40 µg/dL

≥ 80 Urgent medical evaluation and consultation indicated

Osha requirements may apply

Chelation not indicated unless BLL > 50 µg/dL with significant symptoms

Osha requirements may apply

Chelation may be indicated if symptomatic and/or BLL ≥ 100 µg/dL

Table 3. Recommended interpretive guidance for clinical laboratories reporting adult blood lead concentrations.

BLL, blood lead level. Primary management of lead poisoning is source identification and removal from exposure. A single BLL does not reflect cumulative body burden or predict long-term effects.

*Refer to OSHA general industry and construction lead standards for occupational exposure.

References

Aksesson A, Lundh T, Vaher M, Bjellner, Lofiedt J, Norbrand, C, et al. 2005. Tubular and glomerular kidney effects in Swedish women with low environmental cadmium exposure. Environ Health Perspect 113:1627–1631.

Barth A, Schaffer AW, Osterode W, Winker R, Konnaris C, Valic E, et al. 2002. Reduced cognitive abilities in lead-exposed men. Int Arch Occup Environ Health 75:394–398.

Borja-Arbuto VH, Hertz-Picciotto I, Lopez MR, Farias P, Rios C, Blanco J. 1999. Blood lead levels measured prospectively and risk of spontaneous abortion. Am J Epidemiol 150:590–597.

CDC. 2002. Managing Elevated BLLs Among Young Children. Atlanta:Centers for Disease Control and Prevention, National Center for Environmental Health.

CDC. 2005. Third National Report on Human Exposure to Environmental Chemicals. NCEH Publ no 05-0570. Atlanta:Centers for Disease Control and Prevention.

Chung HY, Cho AO, Tsai SY. 2005. Reversible neurobehavioral performance with reductions in blood lead levels—a prospective study on lead workers. Neurotox Teratol 27:497–504.

Chung HY, Schwartz J, Gonzalez-Cossio T, Lugo MC, Palazuelos E, Ara A, et al. 2001. Interrelations of lead levels in bone, venous blood, and umbilical cord blood with exogenous lead exposure through maternal plasma lead in peripartum women. Environ Health Perspect 109:527–532.

Coyle P, Kosnett MJ, Hopkins KL. 2005. Severe lead poisoning in the plastics industry: a report of three cases. Am J Ind Med 47:172–175.

Cremin JD, Luck ML, Laughlin NK, Smith DR. 1999. Efficacy of succimer chelation for reducing brain lead in a primate model of human lead exposure. Toxicol Appl Pharmacol 161:283–293.

Den Hond E, Naesens L, Steessen JA. 2002. The relationship between blood pressure and blood lead in NINHANS III. National Health and Nutritional Examination Survey. J Hum Hypertens 16:563–568.

Dietrich KN, Ware JH, Salgankia, Kredilf J, Rogan WJ, Rhoads GG, et al. 2004. Effect of chelation therapy on the neuropsychological and behavioral development of lead-exposed children after school entry. Pediatrics 114:19–26.

Ettinger AS, Telles-Rojo MM, Amarasiriwardena C, Peterson KE, Schwartz J, Ara A, et al. 2006. Influence of maternal bone lead burden and calcium intake on levels of lead in breast milk over the course of lactation. Am J Epidemiol 163:46–56.
Ettinger AS, Teller-Jojo MM, Amarasiriwardena C, Bellinger D, Peterman J, Schwingt J, Hu H, Hernandez-Avila M. 2004a. Estimation of birth effect of lead on infant blood lead levels at 1 month of age. Environ Health Perspect 112:1381–1385.

Ettinger AS, Teller-Jojo MM, Amarasiriwardena C, Gonzalez-Cossio T, Petreas RJ, Koss MN. 2001. Levels of lead in breast milk and their relation to maternal blood and bone lead levels at one-month postpartum. Environ Health Perspect 112:920–931.

Fine BP, Chang T, Stuckey J, T. A. 1988. Blood pressure elevation in young dogs during low-level lead poisoning. Toxicol Appl Pharmacol 93:388–393.

Gerhardsson L, Chettri DK, Engrav G, Nordberg NG, Nyholm H, Scott D, Jones AD. 2001. Kidney effects in long-term exposed lead smelter workers. Br J Ind Med 49:186–192.

Goldstein GW, Ashbury AK, Diamond I. 1974. Pathogenesis of lead encephalopathy. Uptake of lead and reaction of brain capillaries. Arch Neurol 31:382–389.

Gonzalez-Cossio T, Peterson KE, Sanin LI, Fishbein SE, Palazuelos E, Aro A, et al. 1997. Decrease in birth weight in relation to maternal bone lead burden. Pediatrics 100:496–492.

Gomaa A, Hu H, Bellinger D, Schwartz J, Tsaih S, Gonzalez-Cossio T, et al. 2001. Maternal blood as an independent risk factor for fetal neurotoxicity: a prospective study. Pediatr 111:247–251.

Gonick HC, Ding Y, Bondy SC, Ni Z, Vaziri ND. 1997. Lead-induced hypertension: interplay of nitric oxide and reactive oxygen species. Hypertension 30:1487–1494.

Golson BL, Jameson CW, Mahaffey KR, Mizon KJ, Pausten JA, Law A, et al. 1998. Relationship of lead in breast milk to blood, urine, and diet of the infant and mother. Environ Health Perspect 106:687–694.

Golson BL, Mizon KJ, Kosnett MJ, Mahaffey KR, Taylor AJ. 2001. Dietary intakes of selected elements from longitudinal 6-day duplicate diets for pregnant and nonpregnant subjects and elemental concentrations of breast milk and infant formula. Environ Res 87:160–170.

Hänninen H, Alito A, Kovala T, Luukkonen R, Matikainen E, Mannelin T, et al. 1998. Occupational exposure to lead and neuropsychological dysfunction. Occup Environ Med 55:202–209.

Harlan WR. 1988. The relationship of blood lead levels to blood pressure in the U.S. population. Environ Health Perspect 78:13–17.

Hernandez-Avila M, Peterson KE, Gonzalez-Cossio T, Sanin LH, Aro A, Sanas et al. 2002. Effect of maternal bone on length and head circumference at birth. Arch Environ Health 57:482–488.

Hertz-Picciotto I. 2000. The evidence that leads the increase that is responsible for spontaneous abortion. Am J Ind Med 38:300–309.

Hikins KI, Materna BL, Payne S, Kirsch L. 2004. Family lead point. Clin Pediatr. 43:895–899.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

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Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.

Hofreuter DH, Catcott EJ, Keenan RG, Xintaras C. 1961. The relationship between blood lead, blood pressure during pregnancy with increased bone lead. Arch Environ Health 6:78–82.
Tsaih SW, Korrick S, Schwartz J, Amarasiriwardena C, Aro A, Sparrow D, et al. 2004. Lead, diabetes, hypertension, and renal function: Normative Aging Study. Environ Health Perspect 112:1178–1182.

U.S. EPA. 2006. Air Quality Criteria for Lead (Final). Washington, DC.U.S. Environmental Protection Agency, National Center for Environmental Assessment. Available: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=158823 [accessed 14 December 2006].

Vaziri ND. 2002. Pathogenesis of lead-induced hypertension: role of oxidative stress. J Hypertens 20(suppl 3):S15–S20.

Wasserman GA, Liu X, Popovac D, Factor-Litvak P, Kline J, Watermael C, et al. 2000. The Yugoslavia prospective lead study: contributions of prenatal and postnatal lead exposure to early intelligence. Neurotoxicol Teratol 22:811–818.

Wasserman GA, Liu X, Popovac D, Factor-Litvak P, Kline J, Watermael C, et al. 2000. The Yugoslavia prospective lead study: contributions of prenatal and postnatal lead exposure to early intelligence. Neurotoxicol Teratol 22:811–818.

Weaver VM, Lee BK, Todd AC, Ahn KD, Shi W, Jaar BG, et al. 2006. Effect modification by δ-aminolevulinic acid dehydratase, vitamin D receptor, and nitric oxide synthase gene polymorphisms on associations between patella lead and renal function in lead workers. Environ Res 102:61–69.

Weisskopf MG, Proctor SP, Wright RO, Schwartz J, Spiro A, Sparrow D, Nie H, Hu H. 2007. Cumulative lead exposure and cognitive performance among elderly men. Epidemiology 18:59–66.

Weisskopf MG, Wright RD, Schwartz J, Spiro III A, Sparrow D, Aro A, et al. 2004. Cumulative lead exposure and prospective change in cognition among elderly men: the VA Normative Aging Study. Am J Epidemiol 160:1184–1193.

Winker R, Barth A, Ponocny-Seliger E, Pilger A, Osterode W, Rudiger HW. 2005. No cognitive deficits in men formerly exposed to lead. Wein Klin Wochenschr 117:755–760.

Winker R, Ponocny-Seliger E, Rudiger HW, Barth A. 2006. Lead exposure levels and duration of exposure absence predict neurobehavioral performance. Int Arch Occup Environ Health 79:123–127.

Wright RO, Tsaih SW, Schwartz J, Spiro A, McDonald K, Weiss ST, et al. 2003. Lead exposure biomarkers and mini-mental status exam scores in older men. Epidemiology 14:713–718.

Wu MT, Kelsey K, Schwartz J, Sparrow D, Weiss S, H. 2003. A δ-aminolevulinic acid dehydratase (ALAD) polymorphism may modify the relationship of low level lead exposure to uricemia and renal function: the Normative Aging Study. Environ Health Perspect 111:335–341.