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Health effects of a blood lead level below 10 µg/dL in both adults and children and even below 1 µg/dL in pregnancy

Researched, collated and summary statements chosen by Anne Roberts, Elizabeth O'Brien and Robert Taylor, The LEAD Group Inc, Australia, 17th August 2009; last amended 8th September 2020, by JustOne Lead Soldier.

NB µg/dL (often written as ug/dL) = micrograms per decilitre, and µmol/L (or umol/L) = micromoles per litre, are the usual units used for lead in blood results. Also see "Blood lead testing: who to test, when, and how to respond to the result" at <https://lead.org.au/fs/fst46.html>

Research into the health effects of a blood lead level below 10 µg/dL in adults

1. "Blood Lead Below 0.48 µmol/L (10 µg/dL) and Mortality Among US Adults" by Andy Menke, Paul

Muntner, Vecihi Batuman, Ellen K. Silbergeld and Eliseo Guallar, in Circulation - Journal of the American Heart

Association, September 26, 2006 published online Sep 18, 2006;

<http://circ.ahajournals.org/cgi/content/short/114/13/1388>

“Conclusions—The association between blood lead levels and increased all-cause and cardiovascular mortality was observed at substantially lower blood lead levels than previously reported. Despite the marked decrease in blood lead levels over the past 3 decades, environmental lead exposures remain a significant determinant of cardiovascular mortality in the general population, constituting a major public health problem.”

2. " 'Safe' levels of lead may not be that safe after all" by Melissa Healy, Times Staff Writer, The Los Angeles Times 2/10/06 at <http://articles.latimes.com/2006/oct/02/health/he-lead2>

RE: the above Menke et al study published in the American Heart Association Journal “Circulation”, Sep 18, 2006:

“Researchers used a comprehensive national health survey of American adults to track 13,946 subjects for 12 years and looked at the relationship of blood lead levels and cause of death. They

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found that compared with adults with very low levels of lead in their blood [less than 1.94 micrograms per decilitre], those with blood lead levels of 3.6 to 10 micrograms of lead per deciliter of blood were two and half times more likely to die of a heart attack, 89% more likely to die of stroke and 55% more likely to die of cardiovascular disease. The higher the blood lead levels, the greater the risk of death by stroke or heart attack.

“The dangers of lead held steady across all socioeconomic classes and ethnic and racial groups, and between men and women.”

3. "Lead in Blood: 'Safe' Levels Too High? Average Americans Tested Had Level High Enough for Increased

Heart Disease Death Risk" by Miranda Hitti, Medical Writer, WebMD Medical News, Reviewed By Louise Chang, MD Medical Editor, WebMD Medical News, Sept. 18, 2006 at

<http://www.webmd.com/news/20060918/lead-in-blood-safe-levels-too-high>

“The average blood level of lead found among Americans is high enough to increase the likelihood of heart attack and stroke, according to a new study.

“In fact, people with only a fifth the level of lead in their blood now considered 'high' are more likely to die of heart attack or stroke, the study shows.

“These findings suggest the threshold for 'high' blood levels of lead may not fully take into account lead's heart risks, according to the study.

“The study appears in Circulation's rapid access online edition.”

“A 'high' blood level is now defined as more than 10 micrograms of lead per deciliter of blood (10 mcg/dL).

“Most Americans -- 99% -- fall below that threshold, write the researchers, who include Andy Menke, MPH, of Tulane University School of Public Health.

“But an increased likelihood of death from heart attack or stroke has started to be seen in people with blood levels greater than 2 mcg/dL, according to Menke and colleagues.”

4. "Lead, Cadmium, Smoking, and Increased Risk of Peripheral Arterial Disease" by A Navas-Acien, E Selvin, R Sharrett, E Calderon-Aranda, E Silbergeld, E Guallar in Circulation Issue 109, American Heart Association (AHA) Inc. June 7th 2004.

<http://circ.ahajournals.org/cgi/content/full/109/25/3196>

“This study concluded that blood lead and cadmium, at levels well below current safety standards, were associated with an increased prevalence of peripheral arterial disease in the general US population. Cadmium may partially mediate the effect of smoking on peripheral arterial disease.”

5. "'Safe' levels of lead, cadmium" by Carole Bullock 'Safe' levels of lead, cadmium AHA Journal News report, 8th June 2004, at www.eurekalert.org/pub_releases/2004-06/aha-lo060304.php

“The general public can be exposed to lead and cadmium through cigarette smoke, in ambient air near industrial and combustion sources, in certain foods and sometimes in drinking water. Peripheral artery disease or PAD affects 8 to 12 million Americans, according to the American Heart Association. It is a condition similar to coronary artery disease and carotid artery disease. In PAD, fatty deposits build up in artery walls and reduce blood circulation, mainly in arteries to the legs and feet. In its early stages a common symptom is cramping or fatigue in the legs and buttocks during activity. Such cramping subsides when the person stands still.

“In a study of 2,125 adults, those with the highest blood concentrations of lead or cadmium were almost three times more likely to develop PAD than those with the lowest levels of the two metals. Yet the highest levels were well within what is currently considered safe levels, said senior author Eliseo Guallar, M.D., DrPH, an assistant professor of epidemiology at the Johns Hopkins University Bloomberg School of Public Health in Baltimore. “

6. "Blood Lead Levels and Death from All Causes, Cardiovascular Disease, and Cancer: Results from the NHANES III Mortality Study" by Susan E. Schober, Lisa B. Mirel, Barry I. Graubard, Debra J. Brody, Katherine M.

Flegal in Environmental Health Perspectives Online 6th July 2006, The National Institute of Environmental Health Sciences, National Institutes of Health, U.S. Department of Health and Human Services, 1st Oct 2006, at www.ncbi.nlm.nih.gov/pmc/articles/PMC1626441/

“CONCLUSION: In a nationally representative sample of the U.S. population, blood lead levels as low as 5–9 µg/dL were associated with an increased risk of death from all causes, cardiovascular disease, and cancer.”

7. "Research Indicates that Low Blood Lead Levels Contribute to Early Death from Cardiovascular Disease and Cancer" by Courtney Hinton, Intern at the Alliance for Healthy Housing, & Student, University of Maryland, published in Alliance Alert, August 2006, published by the Alliance for Health Housing (AFHH) at www.afhh.org/res/res_alert_archives_aug06.htm#lowbllearlydeath

This is a summary of item 6, above (The 3rd US National Health and Nutrition Examination Survey, NHANES 3)

“Previous surveys, conducted in 1976–1980, indicated a higher risk of death with blood lead levels higher than 20 µg/dL. Blood lead levels have significantly decreased since 1970, however, and the third survey, conducted from 1988–1994, reflect that even low blood lead levels, between 5–9 µg/dL, carry an increased risk of death.

“The current NHANES, with data from 1999–2002, suggests an elevated risk of peripheral arterial disease, hypertension, and renal dysfunction in a population with blood lead levels averaging approximately 2 µg/dL.

“The analysis of the third NHANES study supports other evidence of adverse health consequences related to blood levels that are lower than current levels of concern.”

8. "Association of blood lead concentrations [greater than 8 µg/dL] with mortality in older women: a prospective cohort study" by Naila Khalil , John W Wilson , Evelyn O Talbott , Lisa A Morrow , Marc C Hochberg , Teresa A Hillier , Susan B Muldoon , Steven R Cummings and Jane A Cauley (2009) at www.ehjournal.net/content/8/1/15

“Methods

Prospective cohort study of 533 women aged 65–87 years enrolled in the Study of Osteoporotic Fractures at two US research centers (Baltimore, MD; Monongahela Valley, PA) from 1986–1988. Blood lead concentrations were determined by atomic absorption spectrometry. Using blood lead concentration categorized as < 8 µg/dL, and ≥ 8 µg/dL, we determined the relative risk of mortality from all cause, and cause-specific mortality, through Cox proportional hazards regression analysis.

“Conclusion

Women with blood lead concentrations of ≥ 8 µg/dL (0.384 µmol/L), experienced increased mortality, in particular from CHD as compared to those with lower blood lead concentrations.”

9. "Association Between Essential Tremor and Blood Lead Concentration" by ED Louis, EC Jurewicz, LK Applegate, P Factor-Litvak, M Parides, L Andrews, V Slavkovich, JH Graziano, S Carroll, and Todd, at www.ncbi.nlm.nih.gov/pmc/articles/PMC1241711/pdf/ehp0111-001707.pdf

“Essential tremor (ET) is a neurologic disease that is characterized by an action tremor of the hands and/or head. ET is considered to be distinct from age-related enhanced physiologic tremor.”

“There was a correlation between the total tremor score and BPb concentration (Spearman’s $r = 0.14$; $p = 0.03$) in the 243 study subjects.”

“BPb concentrations were higher in ET patients than in controls (mean ± SD, 3.3 ± 2.4 and 2.6 ± 1.6 µg/dL, respectively; median, 2.7 and 2.3 µg/dL; $p = 0.038$).”

“In this case–control study, we found that the BPb concentration was higher in ET patients than in controls. This association between higher BPb concentration and the diagnosis of ET persisted after adjusting for confounding variables. The association was strongest in patients with sporadic ET, that is, those with no family history of tremor, suggesting that lead as a toxicant might be of more relevance in ET patients without a genetic susceptibility for ET.”

“Although our data demonstrate an association between ET and higher BPb concentrations, one must be cautious about the interpretation of these data. It is unlikely that a BPb concentration of 3.3 µg/dL alone is sufficient to cause ET.”

10. “Maternal Blood Lead Levels and the Risk of Pregnancy Induced Hypertension. The “EDEN” Cohort Study” by Chadi Yazbeck, Olivier Thiebaugeorges, Thierry Moreau, Valérie Goua, Ginette Debotte, Josiane Sahuquillo, Anne Forhan, Bernard Foliguet, Guillaume Magnin, Rémy Slama, Marie-Aline Charles, Guy Huel. Environmental Health Perspectives, online 26 June 2009, <http://ehp03.niehs.nih.gov/article/submitArticle.action?articleURI=info:doi/10.1289/ehp.0800488>

Results: pregnancy-induced hypertension (PIH) was diagnosed in 106 subjects (10.9%). Age, parity, weight gain, alcohol, smoking habits and calcium supplementation were comparable between hypertensive and non hypertensive women. Lead levels were significantly higher in PIH cases (2.2 µg/dL [0.11 µmol/L] SD 1.4 µg/dL) than in normotensive patients (1.9 µg/dL [0.09 µmol/L] SD 1.2 µg/dL); p=0.02.

Discussion: We found that the adjusted risk of PIH was associated with maternal blood lead levels in midpregnancy. This risk was doubled in the highest quartile as compared to the lowest quartile of lead distribution... Our findings that lead may have an etiologic role in PIH, even at low levels of environmental exposure, suggest that it may be appropriate for public health organizations to consider lowering the upper limit of “acceptable” blood lead levels in pregnant women, which is currently at 10 µg/dL.

11. “Blood lead and preeclampsia: A meta-analysis and review of implications” by Arthur E. Poropat, Mark A. S. Laidlaw, Bruce Lanphear, Andrew Ball, Howard W. Mielke in Environmental Research Volume 160, January 2018, Pages 12-19, at <https://doi.org/10.1016/j.envres.2017.09.014>

[According to the Mayo Clinic, at <https://www.mayoclinic.org/diseases-conditions/preeclampsia/symptoms-causes/syc-20355745> : “Preeclampsia is a pregnancy complication characterized by high blood pressure and signs of damage to another organ system, most often the liver and kidneys.”

A 4th Sept 2017 Griffith University media release at https://lead.org.au/Durack_Lead_poisoning_is_the_top_risk_factor_for_preeclampsia_says_Griffith_study_20171004.pdf - about this Poropat et al (2018) study - states:

Pre-eclampsia is a disease which kills over 75,000 women internationally each year and is responsible for 9% of all fetal deaths.

“We found that the link between high blood lead levels and pre-eclampsia is twice as strong as the risk from diabetes and is as big a risk as chronic high blood pressure,” says Dr Poropat.

“There is a clear dose-response relationship between maternal blood lead and pre-eclampsia: doubling the blood lead level results also doubles the risk of pre-eclampsia. Even relatively low levels of lead increase the risk of the condition.”]

“Increase of 1 µg/dL in BPb results in a 1.6% increase in likelihood of preeclampsia.”

“Odds ratio for BPb and preeclampsia = 9.81 (95% CI = 8.01–12.02).”

“ Women with concentrations higher than 5 µg/dL should be actively monitored”

“95% of lead absorbed into the body is stored in human bones in place of calcium. During pregnancy (especially the third trimester) and lactation, as maternal bones release calcium to the mother’s blood to support fetal development, maternal bones also release lead, thereby exposing the women and the fetus to an even greater exposure risk (Gulson et al., 2016).”

“studies have shown that lead exposure is associated with gestational hypertension”

“The picture that emerges is that BPb is a major risk factor for preeclampsia”

“calcium supplementation may ameliorate maternal hypertension and preeclampsia by suppressing mobilisation of skeletal lead.”

“tests of BPb should be routine when there is suspected environmental or occupational exposure to lead”

“All pregnant women should be encouraged to limit potential exposure to lead contamination, such as by only consuming lead-free water and suppressing household dust.”

Research into the health effects of a blood lead level above 1 µg/dL and below 10 µg/dL in children

12. “Cognitive Deficits Associated with Blood Lead Concentrations <10 microg/dL in US Children and Adolescents” by Lanphear BP, Dietrich K, Auinger P, Cox C. Public Health Rep. 2000;115:521–529, www.ncbi.nlm.nih.gov/pmc/articles/PMC1308622/pdf/pubhealthrep00019-0027.pdf

“Results:: For every 1 µg/dL increase in blood lead concentration, there was a 0.7-point decrement in mean arithmetic scores, an approximately 1-point decrement in mean reading scores, a 0.1-point decrement in mean scores on a measure of nonverbal reasoning, and a 0.5-point decrement in mean scores on a measure of shortterm memory. An inverse relationship between blood lead concentration and arithmetic and reading scores was observed for children with blood lead concentrations lower than 5.0 µg/dL.

“Conclusion. Deficits in cognitive and academic skills associated with lead exposure occur at blood lead concentrations lower than 5 µg/dL.

13.”Intellectual impairment in children with blood lead concentrations below 10 µg per deciliter” by Canfield RL, Henderson CR Jr, Cory-Slechta DA, Cox C, Jusko TA, Lanphear BP, N Engl J Med. 2003;348:1517–1526. AVAILABLE TO SUBSCRIBERS AND PURCHASERS AT <http://content.nejm.org/cgi/content/full/348/16/1517>

The findings of this study are startling and counter-intuitive: at lower concentrations of lead in the blood – below 10µg/dL - children tested for IQ at ages three and five, showed greater decline in IQ than those with higher concentrations- over 10 µg/dL.

“The blood lead concentration was inversely and significantly associated with IQ. In the linear model, each increase of 10 µg per deciliter in the lifetime average blood lead concentration was associated with a 4.6-point decrease in IQ (P=0.004), whereas for the subsample of 101 children whose maximal lead concentrations remained below 10 µg per deciliter, the change in IQ associated with a given change in lead concentration was greater. When estimated in a nonlinear model with the full sample, IQ declined by 7.4 points as lifetime average blood lead concentrations increased from 1 to 10 µg per deciliter.”

14. “Even Low Lead Levels Pose Perils for Children”, by Jane E Brody, New York Times, 5th August 2003, www.nytimes.com/2003/08/05/health/nutrition/05BROD.html This is an interview about the Canfield et al study above.

Since 1923 it has been known that lead damages the brain. Progressively, it has been shown that lower blood lead levels than first thought, causes significant damage to the developing brain.

“Repeatedly over 30 years, follow-up studies of lead-exposed children have demonstrated I.Q. reductions and other memory and learning disturbances associated with successively lower blood lead levels...

“Dr. Needleman and Dr. David C. Bellinger of Boston Children's Hospital and the Harvard Medical School studied 249 mostly middle-class children in the Boston metropolitan region, measuring blood levels levels seven times from birth to age 10.

“Prompted by the Canfield study, they reanalyzed findings among the children whose blood levels never rose above 10 micrograms and found the same effects — proportionately greater harm at the lowest levels.

“Dr. Canfield said in an interview: "Our research suggests that nontrivial damage is occurring below the C.D.C. level of concern. Both the C.D.C. and the World Health Organization need to reassess their policies in light of this research."

Brody also refers to studies linking early childhood exposure to lead and subsequent delinquent behaviour.

15. **"Bellinger DC, Needleman HL. Intellectual impairment and blood lead levels"**. N Engl J Med. 2003; 349:502. www.nejm.org/doi/full/10.1056/NEJM200307313490515

"In the light of the report on intellectual impairment and blood lead levels by Canfield et al... we reanalyzed data from our prospective cohort study, focusing on 48 children whose blood lead levels never exceeded 10 µg per deciliter at birth or at 6, 12, 18, 24, 57, or 120 months. The IQ at 120 months was inversely related to the lead level at 24 months with adjustment for covariates ...[and] analyses suggested that the inverse association persisted at blood lead levels below 5 µg per deciliter."

16. **"Blood Lead Concentrations < 10 µg/dL and Child Intelligence at 6 Years of Age"** by Todd A. Jusko, Charles R. Henderson Jr., Bruce P. Lanphear, Deborah A. Cory-Slechta, Patrick J. Parsons, and Richard L. Canfield, Environmental Health Perspectives - VOLUME 116, NUMBER 2, February 2008, <http://ehp03.niehs.nih.gov/article/fetchArticle.action?articleURI=info:doi/10.1289/ehp.10424>

"Compared with children who had lifetime average blood lead concentrations < 5 µg/dL, children with lifetime average concentrations between 5 and 9.9 µg/dL scored 4.9 points lower on Full-Scale IQ."

17. **"Exposures to Environmental Toxicants and Attention Deficit Hyperactivity Disorder in US Children"** by Joe Braun, Robert S. Kahn, Tanya Froehlich, Peggy Auinger and Bruce P. Lanphear in Environmental Health Perspectives - ehp online.org at <http://ehp03.niehs.nih.gov/article/fetchArticle.action?articleURI=info:doi/10.1289/ehp.9478>

The study found that prenatal exposure to environmental tobacco smoke (ETS – also known as "passive smoking") and environmental lead was found to be a risk factor for attention deficit hyperactivity disorder (ADHD).

18. **"Study: ADHD cases linked to lead, smoking"** by LINDSEY TANNER, Associated Press Medical Writer, www.letsmakeleadhistory.org/LinkClick.aspx?link=News%2fADHDCases.pdf&tabid=71

This is a newspaper report on the preceding item.

"About one-third of attention deficit cases among U.S. children may be linked with tobacco smoke before birth or to lead exposure afterward, according to provocative new research.

"Even levels of lead the government considers acceptable appeared to increase a child's risk of having attention deficit hyperactivity disorder, the study found.

"It builds on previous research linking attention problems, including ADHD, with childhood lead exposure and smoking during pregnancy, and offers one of the first estimates for how much those environmental factors might contribute.

"It's a landmark paper that quantifies the number of cases of ADHD that can be attributed to very important environmental exposures,' said Dr. Leo Trasande, assistant director of the Center for Children's Health and the Environment at Mount Sinai School of Medicine in New York.

"More importantly, the study bolsters suspicions that low-level lead exposure previously linked to behavior problems "is in fact associated with ADHD," said Trasande, who was not involved in the research."

19. **"Exposure Assessment: Lead Neurotoxicity - Is the Center for Disease Control's goal to reduce lead below 10µg/dL blood in all children younger than 72 months by 2010, good enough?"** by Thomas F. Schrager, Ph.D., Toxicology Source published by Cambridge Toxicology Group Inc. at www.toxicologysource.com/toxmed/lead/braininjury.html

Summarises various research papers. Concludes, amongst other things, that "additional data and new analysis of existing data support a growing scientific consensus that a threshold for lead neurotoxicity in fetuses and young children does not exist (WHO 1995; CDC (US Center for Disease Control) 2003); CDC stated in a consensus report that 'a threshold for harmful effects of lead remains

unknown' (Myer et al 2003). And following the release of the comprehensive 'Third National Report on Exposure to Chemicals in Humans' (CDC 2005), Jim Pirkle, deputy director of CDC's Environmental Health Lab, stated unequivocally that a safe blood lead level in children simply does not exist. "

20. **"No "safe" lead level seen for fetal brain"** by Amy Norton, Reuters, originally published January 19, 2006 www.health.state.nm.us/eheb/rep/lead/fetal%20lead.pdf

This is a news report on Schnaas et al (2006), below.

"NEW YORK (Reuters Health) – Exposure to even small amounts of lead through a mother's blood may harm the brain development of unborn babies, a new study suggests.

"The Centers for Disease Control and Prevention (CDC) currently considers 10 micrograms per deciliter ($\mu\text{g}/\text{dL}$) the "level of concern" for lead in the bloodstream, but researchers in Mexico found that maternal blood lead levels well below 10 $\mu\text{g}/\text{dL}$ appeared to have a lasting impact on their children's IQ, at least up to the age of 10."

21. **"Reduced Intellectual Development in Children with Prenatal Lead Exposure"** by L Schnaas, SJ Rothenberg, M-F Flores, S Martinez, C Hernandez, E Osorio, S Ruiz Velasco & E Perroni, EHP 114(5) May 2006, at <http://ehp03.niehs.nih.gov/article/fetchArticle.action?articleURI=info:doi/10.1289/ehp.8552>

"The fetal brain seems susceptible to lower lead concentrations than those established by the official Mexican standard and current CDC guidelines, and the effects are obvious at least until 10 years of age. Although these findings should be replicated, our data suggest that we should establish lower action limits for lead exposure of reproductively active women."

22. **"Association Of Dental Caries And Blood Lead Levels"** by Moss, Mark E; Lanphear, Bruce P; and Auinger, Peggy, at www.lead.org.au/lanv7n4/L74-12.html

"Results The log of blood lead level was significantly associated with the number of affected surfaces for both deciduous and permanent teeth in all age groups, even after adjusting for socio-demographic characteristics, diet, and dental care. Among children aged 5 to 17 years, a 0.24 $\mu\text{mol}/\text{L}$ (5 $\mu\text{g}/\text{dL}$) change in blood lead level was associated with an elevated risk of dental caries (odds ratio, 1.8; 95% confidence interval, 1.3-2.5). Differences in blood lead level explained some of the differences in caries prevalence in different income levels and regions of the United States..."

"Conclusions: Environmental lead exposure is associated with an increased prevalence of dental caries in the US population. Findings may help explain the distribution of caries by income and region of the United States."

23. **"The Relationship between Early Childhood Blood Lead Levels and Performance on End-of-Grade Tests"** by Marie Lynn Miranda, Dohyeong Kim, M. Alicia Overstreet Galeano, Christopher J. Paul, Andrew P. Hull, and S. Philip Morgan at <http://ehp03.niehs.nih.gov/article/fetchArticle.action?articleURI=info:doi/10.1289/ehp.9994>

Conclusions: "using a variety of modeling approaches, blood lead levels in early childhood are related to educational achievement in early elementary school as measured by performance on end-of-grade testing. According to 2003–2004 NHANES data, 50% of children 1–5 years old nationwide are estimated to have blood lead levels of $\geq 3 \mu\text{g}/\text{dL}$ (National Center for Health Statistics 2006). Thus as many as half the children in the United States are experiencing negative effects associated with lead exposure—a significantly higher proportion than the 2.3% estimated using the CDC's current blood lead action level of 10 $\mu\text{g}/\text{dL}$. In addition, early childhood lead exposures appear to have more impact on performance on the reading than on the mathematics portions of the EOG, although the differences may not be statistically significant. This differential impact on reading versus mathematics is consistent with previous studies (Fulton et al.1987; Lanphear et al. 2000)."

24. **"Low Blood Lead Levels Associated with Clinically Diagnosed Attention-Deficit/Hyperactivity Disorder and Mediated by Weak Cognitive Control"** by Joel T. Nigg , G. Mark Knottnerus, Michelle M. Martel, Molly Nikolas, Kevin Cavanagh, Wilfried Karmaus,

“Blood lead levels in this sample closely matched US population exposure averages, with a maximum level of 3.4 µg/dL. Blood lead levels were statistically significantly higher in ADHD-combined type than in non-ADHD control ($p < .05$) children. Blood lead was associated with symptoms of hyperactivity-impulsivity but not inattention-disorganization, after control of covariates. Blood lead levels were linked with a lower IQ ($p < .05$), but IQ did not account for effects on hyperactivity. Instead, hyperactivity mediated effects of lead on IQ. Effects of blood lead on hyperactivity-impulsivity were mediated by poor performance on the stop task. This mediation effect was independent of effects of lead on IQ.

Conclusions

“Low-level lead exposure might be an important contributor to ADHD. Its effects seem to be mediated by less effective cognitive control, consistent with a route of influence via striatal-frontal neural circuits.”

25. “Low-Level Environmental Lead Exposure and Children's Intellectual Function: An International Pooled Analysis” BP. Lanphear, R Hornung, J Khoury, K Yolton, P Baghurst, DC. Bellinger, RL. Canfield, KN. Dietrich, R Bornschein, T Greene, SJ. Rothenberg, HL. Needleman, L Schnaas, G Wasserman, J Graziano, R Roberts Environ Health Perspect. 2005 July; 113(7): 894–899. at www.ncbi.nlm.nih.gov/pmc/articles/PMC1257652/

“For a given increase in blood lead, the lead-associated intellectual decrement for children with a maximal blood lead level < 7.5 µg/dL was significantly greater than that observed for those with a maximal blood lead level ≥ 7.5 µg/dL ($p = 0.015$). We conclude that environmental lead exposure in children who have maximal blood lead levels < 7.5 µg/dL is associated with intellectual deficits.”

26. “Longitudinal Associations Between Blood Lead Concentrations Lower Than 10 µg/dL and Neurobehavioral Development in Environmentally Exposed Children in Mexico City” Martha M. Teñlez-Rojo, ScDa, David C. Bellinger, PhD_{b,c}, Carmen Arroyo-Quiroz, BSc_a, Héctor Lamadrid-Figueroa, MD_a Adriana

Mercado-García, MD, MPH_a, Lourdes Schnaas-Arrieta, MSc_d, Robert O. Wright, MD, MPH_e, Mauricio Hernández-Avila, MD, ScDa, Howard Hu, MD, MPH, ScD_{c,e} PEDIATRICS Volume 118, Number 2, August 2006 e323-e332 <http://pediatrics.aappublications.org/cgi/reprint/118/2/e323>

“RESULTS. Adjusting for covariates, children’s blood lead levels at 24 months were significantly associated, in an inverse direction, with both Mental Development Index and Psychomotor Development Index scores at 24 months. Blood lead level at 12 months of age was not associated with concurrent Mental Development Index or Psychomotor Development Index scores or with Mental Development Index at 24 months of age but was significantly associated with Psychomotor Development Index score at 24 months. The relationships were not altered by adjustment for cord blood lead level or, in the analyses of 24-month Mental Development Index and Psychomotor Development Index scores, for the 12-month Mental Development Index and Psychomotor Development Index scores. For both Mental Development Index and Psychomotor Development Index at 24 months of age, the coefficients that were associated with concurrent blood lead level were significantly larger among children with blood lead levels < 10 µg/dL than it was among children with levels > 10 µg/dL.

CONCLUSIONS. These analyses indicate that children’s neurodevelopment is inversely related to their blood lead levels even in the range of < 10 µg/dL. Our findings were consistent with a supralinear relationship between blood lead levels and neurobehavioral outcomes.

27. “Deficits in cognitive function and achievement in Mexican first-graders with low blood lead concentrations” [Abstract Only] Katarzyna Kordas, Richard L. Canfield, Patricia López, Jorge L. Rosado, Gonzalo

García Vargas, Mariano E. Cebrián, Javier Alatorre Rico, Dolores Ronquillo and Rebecca J. Stoltzfus Environmental Research Volume 100, Issue 3, Pages 295-442 (March 2006)

“Elevated blood lead levels in children are associated with lower scores on tests of cognitive functioning. Recent studies have reported inverse relations between lifetime exposure and intellectual

functioning at blood lead concentrations below 10 µg/dL, the Centers for Disease Control and Prevention's (CDC) level of concern. We report associations between blood lead and cognitive performance for first-grade Mexican children living near a metal foundry...

“ One implication of [our] findings is that at the age of 7 years, even in the absence of information on lead exposure in infancy and early childhood, a test result with blood lead <10 µg/dL should not be considered safe. Together with other recent findings, these results add to the empirical base of support available for evaluating the adequacy of current screening guidelines and for motivating efforts at primary prevention of childhood lead exposure”

28. “Lead Exposure and Cardiovascular Dysregulation in Children” [Abstract only] James A. MacKenzie,

Brooks B. Gump, Kristen Roosa, Kestas Bendinskas, Amy Dumas, Robert Morgan and Patrick Parsons The FASAB Journal paper presented to The American Physiological Society at the Experimental Biology 2009 conference, New Orleans 18-22 April, 2009 at www.fasebj.org/cgi/content/meeting_abstract/23/1_MeetingAbstracts/786.13

“Increasing lead (Pb) exposure is associated with increased blood pressure in humans and animal studies suggest this is due to increased vascular resistance.”

“The authors looked at cardiovascular reactions to acute stress in 9-11 year old children with low blood levels – below 3.76 µg/dL

“Pb levels were significantly associated with increased total peripheral resistance (TPR) responses and diminished stroke volume and cardiac output responses to AS. This vascular pattern of response to AS tasks may predict future hypertension.”

“The effects described here were significant for Pb levels considered well below the 10 µg/dL threshold set by the CDC (Centers for Disease Control) for deleterious effects.”

29. “Low Lead Levels In Children Can Affect Cardiovascular Responses To Stress” The American Physiological Society press release about the Mackenzie paper above www.the-aps.org/press/releases/09/18.htm

“Even low levels of lead found in the blood during early childhood can adversely affect how the child’s cardiovascular system responds to stress and could possibly lead to hypertension later in life, according to a study from the State University of New York (SUNY) at Oswego.

“Lead exposure was associated with an increase in vascular resistance when the children worked on a stressful computer task. Vascular resistance is a measure of tension within the blood vessels. Increased vascular resistance may lead to hypertension if it continues over time.

“The study also found that lead exposure was associated with a decrease in circulating aldosterone levels. Aldosterone is a hormone that helps regulate blood pressure.

“One of the study’s most important findings is that all of the participants had very low lead levels, well below the 10 micrograms per deciliter that the CDC defines as a level of concern. The highest lead level for the children in this study was 3.8 micrograms per deciliter.

“The interesting thing was that the levels of lead were all pretty low in the children who participated,” Dr. MacKenzie said. “We’re seeing the negative effects at these low levels.”

30. “Gender specific differences in neurodevelopmental effects of prenatal exposure to very low-lead levels: The prospective cohort study in three-year olds” {abstract only}

Wieslaw Jedrychowski, Frederica Perera,

Jeffery Jankowski, Dorota Mrozek-Budzyn, Elzbieta Mroz, Elzbieta Flak, Susan Edwards, Anita Skarupa, Ilona Lisowska-Miszczyk Early Human Development Vol 85, Is 8 Pages 503-510 (August 2009) at [www.earlyhumandevlopment.com/article/S0378-3782\(09\)00077-2/abstract](http://www.earlyhumandevlopment.com/article/S0378-3782(09)00077-2/abstract)

“Conclusion: the study suggests that there might be no threshold for lead toxicity in children and provides evidence that 3-year old boys are more susceptible than girls to prenatal very low lead exposure. The results of the study should persuade policy makers to consider gender-related susceptibility to lead and possibly to other toxic hazards in setting environmental protection

guidelines. To determine whether the cognitive deficit documented in this study persists to older ages, the follow-up of the children over the next several years is to be carried out.”

31. Childhood Lead Poisoning Prevention Too Little, Too Late Bruce P. Lanphear, MD, MPH at <http://jama.ama-assn.org/content/293/18/2274.extract>

“Despite the dramatic decline in children’s blood lead concentrations, lead toxicity remains a major public health problem. Environmental lead exposure in children—typically measured using lead in whole blood or teeth—has been associated with an increased risk for reading problems, school failure, delinquency, and criminal behavior.⁹⁻¹⁴ Moreover, there is no evidence of a threshold for the adverse consequences of lead exposure.^{15,16} Indeed, studies show that the decrements in intellectual function are, for a given increase in blood lead concentration, greater at blood lead levels lower than 10 µg/dL,^{15,16} the level considered acceptable by the CDC.”

32. "Neuropsychological function in children with blood lead levels < 10 µg/dL" by Pamela J. Surkan, Annie

Zhang, Felicia Trachtenberg, David B. Daniel, Sonja McKinlay, David C. Bellinger, in *NeuroToxicology* 28 (2007) 1170-1177 published online 25 July 2007; www.nchh.org/Portals/0/Contents/Article0822.pdf

“Among participants in the NECAT [New England Children’s Amalgam Trial], children with blood lead levels of 5-10 µg/dL had significantly lower scores on IQ, achievement, attention, and working memory than did children in the referent group, who had levels of 1-2 µg/dL.”

“It appeared to be within the domain of executive functioning that the children with lead levels of 5-10 µg/dL showed their most consistent deficits....These findings suggest that working memory, cognitive flexibility, and ability to formulate, test, and adapt hypotheses might contribute to impaired scores on apical tests”

“In summary, we found that blood lead levels of 5-10 µg/dL in school-age children are associated with deficits in intelligence, visual-spatial skills, executive function, and IQ adjusted academic achievement.”

33. "In kids, even a low blood lead level is a concern" By Patricia Many NEW YORK NURSE: July/August

2008 at www.nysna.org/publications/newyorknurse/2008/jul_aug/research.htm

“The study [Surkan and colleagues (2007)] assessed the impact that a BLL ≤10µg/dL had on mental and behavioral development of 534 English-speaking children ages 6-10 from the New England area.”

“[The] battery of tests examines vocabulary, comprehension, picture arrangement, block design, and maze completion... reading, math, and spelling.... fine motor skills, memory, attention, verbal tests, finger tapping, and reaction time.”

“Children with a BLL of 1-2 µg/dL were compared to children with a BLL of 3-4 µg/dL and 5-10 µg/dL. The results indicate that children with a BLL of 5-10 µg/dl scored lower, especially in vocabulary, math, reading, attention span, and working memory.”

34. "Blood lead levels and specific attention effects in young children" by Lisa M. Chiodo, Chandice

Covington, Robert J. Sokol, John H. Hannigan, James Jannise, Joel Ager, Mark Greenwald and Virginia DelaneyBlack in *Neurotoxicology and Teratology* Volume 29, Issue 5, September-October 2007, Pages 538-546 published online 21 April 2007

“Importantly, the present study documents a significant negative impact of blood lead levels on attention, but not impulsivity, in early elementary age children, further delineating the specific aspects of attention related to blood lead concentrations. Analyses were also conducted to identify a "safe" blood lead level threshold. Visual inspection of non-parametric regression plots suggested a gradual linear dose-response relationship for each endpoint. None of the neurobehavioral outcomes assessed showed evidence of a threshold under which lead levels appear to "safe". In light of the consistency

of these findings with those of several other groups, it is advisable to consider whether the threshold for an acceptable blood lead level should be reduced.”

35. “[Effects of early childhood lead exposure on academic performance and behaviour of school age children](#)” by K Chandramouli, C D Steer, M Ellis, A M Emond (2009)

“After adjustment for confounders, blood lead levels at 30 months showed significant associations with educational attainment, antisocial behaviour and hyperactivity scores at age 7–8 years...”

“Blood lead levels >5 µg/dL were associated with reduced Standard Assessment Tests scores, and levels >10 µg/dL with increased scores for antisocial activities and hyperactivity...”

“Conclusions: Exposure to lead early in childhood has effects on subsequent educational attainment, even at blood levels below 10 µg/dL. **These data suggest that the threshold for clinical concern should be reduced to 5 µg/dL.”**

36. “ Blood Lead Levels Well Below “Safe” Threshold Harm Children's Development” from Medical News Today 18 Sep 2009, at www.medicalnewstoday.com/articles/164336.php

“The higher the level of lead in the blood at the age of 30 months, the poorer were reading, writing, and spelling grades on the Standard Assessment Tests (SATS), and the greater were the chances of antisocial behaviour [at 7 and 8 years of age].”

“But lead levels of between 5 and 10 µg/dL were associated with significantly poorer scores for reading (49% lower) and writing (51% lower). A doubling in lead level from 5 to 10 µg/dL was associated with a 0.3 point fall in SAT scores.”

According to **“Cognitive Tests: Interpretation for Neurotoxicity? (Workshop Summary)”** by William Slikker, Jr., Barbara D. Beck, Deborah A. Cory-Slechta, Merle G. Paule, W. Kent Anger and David Bellinger (2000) at <http://toxsci.oxfordjournals.org/content/58/2/222.full.pdf+html> - **“Apical Test Scores Represent Final Common Pathways for the Expression of Diverse Cognitive Patterns:** The assessment battery typically used in a neurotoxicant study consists of a global or apical test, supplemented by tests thought to assess particular aspects of cognition (e.g., language, visual-spatial skills, memory, and fine motor function). Historically, however, it is apical test scores (e.g., full-scale IQ) rather than domain-specific test scores that have received the most attention, most likely because they can more readily be incorporated into risk assessment and cost benefit analyses.”

Health effects of a blood lead level even below 1 µg/dL in pregnancy

37. “Changes in low levels of lead over the course of pregnancy and the association with birth outcomes” by Felicia A. Rabito, Mehmet Kocak, Derek W. Werthmann, Frances A. Tylavsky, Christopher D. Palmer, Patrick J. Parsons in Reproductive Toxicology Volume 50, December 2014, Pages 138-144, published online 22 Oct 2014, at <https://www.sciencedirect.com/science/article/abs/pii/S0890623814002597?via%3Dihub>

“A 0.1 µg/dL increase in second trimester lead was associated with lower birth weight and pre-term birth.”

“Maternal blood lead below 1 µg/dL behaves in a manner similar to lead at higher levels and is associated with a small decrease in birth weight and gestational age.”

“We found that a 0.1µg/dL increase in second trimester lead resulted in a 43 g decrease in birth weight”

“We found that increasing lead in both the second and third trimester was associated with pre-term birth”

“Our results show a statistically significant rise in maternal blood lead from the second trimester to delivery”

“Sample blood lead, $\mu\text{g}/\text{dL}$: n/ Mean(Range)/Geometric Mean(Standard deviation)

- Second trimester 98/ 0.43 (0.19–1.22)/ 0.42 (0.20)
- Third trimester 88/ 0.43 (0.19–2.10)/ 0.45 (0.28)
- Delivery 69/ 0.50 (0.21–2.47)/ 0.50 (0.35)”

“results from this study suggest that prenatal lead exposure may impact birth outcomes at levels previously considered safe”

“Further research on larger population-based cohorts is needed to confirm these findings and to investigate the level at which clinically relevant decrements in birth outcomes occurs.”