GLASS provides information & referrals on lead poisoning & lead contamination prevention & management, with the goal of eliminating lead poisoning globally & protecting the environment from lead. GLASS is run by The LEAD Group Incorporated ABN 25 819 463 114

global lead advice & support service

Dangers of a blood lead level above 2 µg/dL and below 10 µg/dL to children

By Robert Taylor for The LEAD Group Inc, Australia, December 2010

NB µg/dL = micrograms per decilitre, and µmol/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"

1. "Cognitive and Sensorimotor Functions in 6-Year-Old Children in Relation to Lead and Mercury Levels: Adjustment for Intelligence and Contrast Sensitivity in Computerized Testing" by J. Walkowiak, L. Altmann, U. Krämer, K. Sveinsson, M. Turfeld, M. Weishoff-Houben And G. Winneke in Neurotoxicol Teratol. 1998 Sep-Oct;20(5):511-21. www.ncbi.nlm.nih.gov/pubmed/9761589 [Abstract]

"The Centers for Disease Control (CDC) have proposed a population-based pediatric blood lead concentration of 100µg/l [10 µg/dL as a community action level (1991), and the World Health Organization (WHO) has agreed to this standard. … In the present study subtle but statistically significant (p , 0.05) or borderline (p , 0.10) associations between internal lead dose and some neurobehavioral endpoints were found at geometric mean blood lead concentrations of only 42 µg/l with the 95 percentile value not exceeding 90 µg/l.."

2. "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.pubmedcentral.nih.gov/picrender.fcgi?artid=1308622&blobtype=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 short-term 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".

3."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 AT www.nejm.org/doi/full/10.1056/NEJMoa022848

The findings of this study are startling and counter-intuitive: at lower concentrations of lead in the blood – below 10 µg/dL - children tested for IQ at ages three and five, showed a greater decline in IQ for a rise in blood lead from 1 to 10 µg/dL, than those whose blood lead level went from 10 to 20 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."

4. "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.

5. "Bellinger DC, Needleman HL. Intellectual impairment and blood lead levels". N Engl J Med. 2003; 349:502. http://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."

6. "Neurodevelopmental effects of postnatal lead exposure at very low levels" by Lisa M. Chiodo, Sandra W. Jacobson & Joseph L. Jacobson in Neurotoxicology and Teratology 26 (2004) 359–371

"The results of this study show consistent neurobehavioral deficits in relation to low levels of lead exposure in a lower SES, urban sample. These deficits were found in the domains of overall IQ, performance IQ, reaction time,

visual–motor integration, fine motor skills, attention including executive function, off-task behaviors, and withdrawn behaviors on the TRF. Although at least one other study has found deficits in children exposed to levels less than 5 µg/dl, the research presented here identified effects on attention at levels as low as 3 µg/dl."

"At 5 µg/dl, deficits were identified in several domains of IQ (e.g., BD), visual–motor integration, and attention. With the exception of digit span backwards and two sustained attention measures, all endpoints assessed showed a negative association between lead and neurobehavioral outcome at either 5 or 3 µg/dl…This research provides additional support for the conclusion that neurobehavioral deficits are consistently associated with blood lead concentrations below 10 µg/dl …."

7. "Childhood Lead Poisoning Prevention: Too Little, Too Late" by Bruce P. Lanphear, MD, MPH (2005), AVAILABLE FOR PURCHASE at http://jama.ama-assn.org/cgi/content/full/293/18/2274; 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 behaviour. Moreover, there is no evidence of a threshold for the adverse consequences of lead exposure. 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, the level considered acceptable by the CDC."

8. "Association of umbilical cord blood lead with neonatal behavior at varying levels of exposure" by Archana B Patel, Manju R Mamtani, Tushar P Thakre and Hemant Kulkarni in Neural and Brain Functions 2006, 2:22 at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1557521/

"…we estimated the simultaneous indirect effects of umbilical cord blood lead (CBL) levels and other neonatal covariates on the NBAS clusters."

"Results: "We observed that when analyzed in all study subjects, the CBL levels independently and strongly influenced autonomic stability and abnormal reflexes clusters. However, when the analysis was restricted to neonates with CBL <10 µg/dL, CBL levels strongly influenced the range of state ,motor and autonomic stability clusters. Abnormal walking reflex was consistently associated with an increased CBL level irrespective of the cut-off for CBL, however, only at the lower cut-offs were the predominantly behavioral effects of CBL discernible." [Table 3 p8 summarises impacts at CBL of 5,10 and 25 µg/Dl]

"Conclusion: Our results further endorse the need to be cognizant of the detrimental effects of blood lead on neonates even at a low-dose prenatal exposure."

9. "Neurotoxicity and aggressiveness triggered by low-level lead in children: a review" by Kelly Polido Kaneshiro Olympio; Claudia Gonçalves; Wanda Maria Risso Günther; Etelvino José Henriques Bechara in Rev Panam Salud Publica vol.26 no.3 Washington Sept. 2009 at www.scielosp.org/pdf/rpsp/v26n3/11.pdf

"More recent data point toward cognitive, attention and behaviour deficits in children with BLL between 3 and 5 µg/dL (9). In 2007, Chiodo et al. (77) presented data showing that a threshold below which BLL is not associated with harmful outcomes does not exist. The authors suggest a reduction of the "acceptable" level, considering the recent scientific evidence. Dudek and Merecz (90) found that the fastest deterioration of IQ was observed with BLL between 5 and 10 and 11 to 15 µg/dL, consistent with the finding by Schwartz (82) of an increased slope at lower BLL (79)."

10. "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."

11. "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). There is lead in cigarettes and in ETS.

“We conducted secondary analyses to examine the effects of lead exposure at blood lead levels < 5 µg/dL and to test the stability of our results. When the sample was restricted to children with concurrent blood lead concentrations ≤ 5 µg/dL, there was still a significant association between higher blood lead levels and ADHD. Compared with children in the lowest quintile (nondetectable to 0.7 µg/dL), children with blood lead levels in the highest quintile (2.0–5 µg/dL) had a 4.5-fold fold (95% CI, 1.3–15.3) higher risk for ADHD.” Also see item 32

This is a newspaper report on the preceding item, no.11

“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.”

12. "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

13. "Exposure Assessment: Lead Neurotoxicity - Is the Center for Disease Control's goal to reduce lead below 10 µg/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/tox-med/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. “

14. "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 Delaney-Black 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.”

15. "No "safe" lead level seen for fetal brain" by Amy Norton, Reuters, originally published January 19, 2006

This is a news report on Schnaas et al (item 16 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 (µg/dL) the "level of concern" for lead in the bloodstream, but researchers in Mexico found that maternal blood lead levels well below 10 µg/dL appeared to have a lasting impact on their children's IQ, at least up to the age of 10."

16. "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, 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."

17. "Association Of Dental Caries And Blood Lead Levels" by Moss, Mark E; Lanphear, Bruce P; and Auinger, Peggy, at http://jama.ama-assn.org/content/281/24/2294.full.pdf

"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 µmol/L (5 µg/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."

18. "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 ≥ 3 µg/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 µg/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)."

19. "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 http://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."

20. "Reduced Intellectual Development in Children with Prenatal Lead Exposure" by Lourdes Schnaas, Stephen J. Rothenberg, Maria-Fernanda Flores, Sandra Martinez, Carmen Hernandez, Erica Osorio, Silvia Ruiz Velasco and Estela Perroni in EHP 114(5) May 2006 at http://ehp03.niehs.nih.gov/article/info%3Adoi%2F10.1289%2Fehp.8552

"Geometric mean BPb during pregnancy was 8.0 µg/dL (range, 1–33 µg/dL), from 1 through 5 years was 9.8 µg/dL (2.8–36.4 µg/dL), and from 6 through 10 years was 6.2 µg/dL (2.2–18.6 µg/dL). IQ at 6–10 years decreased significantly only with increasing natural-log third trimester BPb (β = –3.90; 95% confidence interval, –6.45 to –1.36), controlling for other BPb and covariates. The dose–response BPb–IQ function was log-linear, not linear–linear."

"Given the modest sample size and relatively low power of this study, we do not claim that lead exposure from 6 to 10 years or any other developmental period has no effect on child IQ. More likely, third-trimester lead exposure is a more powerful predictor of later child IQ and absorbed enough of the variation in IQ formerly attributed to 6- to 10-year BPb to render it insignificant in our model."

"Across a range of BPb from 1 to 32 µg/dL, these data show that half of the deleterious effects of lead on child IQ measured here occurred when third-trimester BPb increased from 1 to 6 µg/dL. When maternal BPb reached current Mexican and U.S. action limits for children and pregnant women (10 µg/dL), most of the adverse consequences on later child IQ associated with lead in the measured range had already occurred. If we continue to accept the current action limit, we also accept that most of the "damage" to the IQ of children associated with third-trimester lead exposure in our sample is permissible."

"Lead exposure around 28 weeks gestation is a critical period for later child intellectual development, with lasting and possibly permanent effects. There was no evidence of a threshold; the strongest lead effects on IQ occurred within the first few micrograms of BPb."

21. "Longitudinal Associations Between Blood Lead Concentrations Lower Than 10 µg/dL and Neurobehavioral Development in Environmentally Exposed Children in Mexico City" Martha M. Te´llez-Rojo, David C. Bellinger, Carmen Arroyo-Quiroz, He´ctor Lamadrid-Figueroa, Adriana Mercado-Garcı´a, Lourdes Schnaas-Arrieta, Robert O. Wright, Mauricio Herna´ndez-Avila and Howard Hu 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."

22. "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"

22. "Association of Prenatal and Childhood Blood Lead Concentrations with Criminal Arrests in Early Adulthood" by John Paul Wright, Kim N. Dietrich, M. Douglas Ris, Richard W. Hornung, Stephanie D. Wessel, Bruce P. Lanphear, Mona Ho, Mary N. Rae in PLoS Medicine May 2008 Vol. 5, Is. 5, e101 at http://www.plosmedicine.org/article/info%3Adoi%2F10.1371%2Fjournal.pmed.0050101

Found significant increases in arrests for crime, particularly violent crime, as adults for individuals whose pre-natal blood lead levels or 6 year blood lead were above 3µg/dl or if their childhood average blood lead was above 6 µg/dl, with increases above 27% for every 5 µg/dl increment: see graphs on p736 and 738.

23. "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, Marsha D. Rappley Biological Psychiatry Vol 63, Is 3,1st February 2008 at http://www.journals.elsevierhealth.com/periodicals/bps/article/PIIS0006322307006750/abstract

"Blood lead levels in this sample closely matched US population exposure averages, with a maximum level of 3.4 µg/d. 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."

Conclusion

"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."

24. "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."

25. "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."

26. "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.earlyhumandevelopment.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."

27. "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) 1170-1177published online 25 July 2007; AVAILABLE at 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."

♦ 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.*

28. "In kids, even a low blood lead level is a concern" By Patricia Many NEW YORK NURSE: July/August 2008 at http://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 behavioural 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."

29. "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), at http://adc.bmj.com/content/94/11/844.abstract

"[Blood Lead] samples were taken … at 30 months of age. … Developmental, behavioural and standardised educational outcomes (Standard Assessment Tests, SATs) were collected on these children at age 7–8 years."

"Treating lead levels categorically, with the reference group 0–2 µg/dl, no effects on outcomes were apparent at 2–5 µg/dl, but levels of 5–10 µg/dl were associated with a reduction in scores for reading (OR 0.51, p=0.006) and writing (OR 0.49, p=0.003). Lead levels >10 µg/dl were also associated with increased scores for antisocial behaviour (OR 2.9, p=0.040) and hyperactivity (OR 2.82,p=0.034)."

"The effect of doubling exposure from 5 to 10 µg/dl caused a decline in SATS scores for writing of 0.2 points (95% CI 20.03 to 20.8). It was also associated with an increase in hyperactivity scores reported by the teacher of 0.3 points (95% CI 20.9 to 0.63)."

"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..."

"Our results are consistent with other studies showing effects on behaviour and cognition of blood lead levels under 10 mg/dl. Although the effects of lead appear small compared to the impact of parenting and social factors on educational attainment, they are detectable many years after exposure. The clinical importance of these findings is that exposure to lead may interact with other environmental factors associated with educational disadvantage to have a cumulative long term impact. Volumetric analyses of whole brain MRI data have shown significant decreases in frontal lobe volume in adulthood associated with childhood blood lead concentrations."

"These data suggest that the threshold for clinical concern should be reduced to 5 µg/dL"

30. "The Long-term Effects of Early Childhood Lead Exposure: Evidence from the Phase-out of Leaded Gasoline" by J Peter Nilsson From Uppsala University and IFAU available at "**sites.google.com/site/valentinyiakos/Home/files/Paper_Nilsson.pdf**" copy and paste into Google search.

" The main results suggest that low levels of lead exposure early in life have both statistically significant and economically important effects on future educational attainments and labor market outcomes. A key finding is a clear nonlinear relationship between local air lead levels in childhood and long-term outcomes at the relatively low levels of exposures considered. Above an estimated municipality average early childhood blood lead level of 5µg/dL, reductions in lead exposure have a consistently positive and significant impact on long-term outcomes. Below this level reductions no longer seems to affect adult outcomes in a consistent or significant direction."

"Further analysis reveals that children from poorer families seem to have benefited most from the gasoline lead reductions…"

"…this study use the average municipality lead levels as exposure measure, the average effects on cognitive ability are associated with a municipality average blood lead level above 4.8µg/dL…a decrease in a child's blood lead level from 10 µg/dL to 5 µg/dL would imply an average increase in 9th grade GPA by 2.2 percentiles and an increase in the high school graduation rate by 2.3 %. In terms of labor market outcomes the same decrease would imply an estimated increase in earnings (average for ages 20-32) by 5.5%."

31. "Children's blood lead and standardized test performance response as indicators of neurotoxicity in metropolitan New Orleans elementary schools" by S. Zahran, H.W. Mielke, S. Weiler , K.J. Berry, C. Gonzalesin in NeuroToxicology Vol. 30, Is. 6, Nov 2009, p 888-897

"Included in the panoply of factors, we observe that BPb is a more powerful predictor of student performance than poverty (offset with free or discounted lunch) and class size."

"In this study the regression coefficients among median BPb and ATS in English, Science, Mathematics and Social Studies range from b ¼ _0:075 to b ¼ _0:082 (p<0:01), indicating that an increase in median BPb of 1 mg/dL reduces school-ATS by about one-tenth of an ATS point."

"The results of this study support recent calls for lowering BPb action levels from 10 to less than 5 or, even 2 mg/dL (Gilbert and Weiss, 2006; Min et al., 2007), and increased emphasis on primary Pb prevention to protect children from the effects of neurotoxicity (Bellinger, 2008; Rogan et al., 2001). Analyzing achievement outcomes as a function of the percentage of children at or below 5 and 2 µg/dL in Table 7, show that ATS in all subject areas are statistically sensitive to the presence of children at or above these lower threshold levels."

32. "Association of Tobacco and Lead Exposures With Attention-Deficit/Hyperactivity Disorder" by Tanya E. Froehlich, Bruce P. Lanphear, Peggy Auinger, Richard Hornung, Jeffery N. Epstein, Joe Braun and Robert S. Kahn in Pediatrics 2009;124;e1054-e1063 at http://pediatrics.aappublications.org/cgi/content/abstract/124/6/e1054 [Follow up article to item 11]

"When the sample was restricted to children with lead concentrations of <5 µg/dL, increasing lead levels were still significantly associated with DSM-IV–defined ADHD; compared with children in the lowest tertile (nondetectable to 0.8 µg/dL), those with lead levels in the highest tertile (>1.3–5 µg/dL) had a more than twofold increased risk of ADHD (a OR for third versus first tertile:2.3[95% CI: 1.4 –3.7])."

33. "Confirmation and Extension of Association of Blood Lead with Attention-Deficit/Hyperactivity Disorder (ADHD) and ADHD Symptom Domains at Population-Typical Exposure Levels" by Nigg JT, Nikolas M, Knottnerus G Cavanagh K and Friderici K from National Institutes of Health 23/1/2010 at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2810427/pdf/nihms140374.pdf

"236 children aged 6–17 years participated (61 ADHD-Combined type, 47 ADHD Predominantly Inattentive type, 99 non-ADHD control, 29 unclassified borderline, situational, or NOS cases)."

"Blood lead levels were slightly below United States and Western Europe population exposure averages, with a mean of 0.73 and a maximum of 2.2 µg/dL. This is the lowest level of blood lead ever studied in relation to ADHD. After statistical control for covariates including IQ and prenatal smoking exposure, blood lead was associated with ADHD-combined type but not inattentive type."

34. "Blood Lead Level and Kidney Function in US Adolescents: The Third National Health and Nutrition Examination Survey [NHANES III]" by Jeffrey J. Fadrowski, Ana Navas-Acien, Maria Tellez-Plaza, Eliseo Guallar, Virginia M. Weaver and Susan L. Furth in Arch Intern Med/Vol 170 (No. 1), Jan 11, 2010 at www.ncbi.nlm.nih.gov/pubmed/20065202

"Participants included 769 adolescents aged 12 to 20 years for whom whole blood lead and serum cystatin C were measured in the Third National Health and Nutrition Examination Survey, conducted from 1988- 1994."

"Among the study participants, the median whole blood lead level was 1.5 µg/dL …In linear regression analyses, higher blood lead levels were consistently associated with a lower cystatin C–estimated GFR Participants with lead levels in the highest quartile (> or = 3.0 µg/dL) had a 6.6 mL/min/ 1.73 m(2)–lower estimated GFR (95% confidence interval [CI], –0.7 to –12.6 mL/min/1.73m(2)) compared with those in the first quartile (lead level <1 µg/dL), with a highly significant test for trend (P=.009). Doubling of blood lead levels was associated with a 2.9 mL/min/1.73 m(2)–lower estimated GFR in the fully adjusted model (95% CI, –0.7 to –5.0 mL/min/1.73 m(2))."

"Previous epidemiologic studies conducted in vulnerable adult populations, such as those with CKD or hypertension, have shown that low-level environmental lead exposure was inversely associated with kidney function in cross-sectional and prospective analyses. Our study extends these findings to a general population sample of US adolescents, indicating that lead exposure at levels common in developed countries is associated with lower kidney function, even in the absence of other comorbidities. Our findings also suggest that previous studies using creatinine-based estimates of kidney function in healthy populations may have substantially underestimated the adverse association of higher blood lead levels on kidney function."

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