



# Lead - from a toxicologist's perspective



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# Aim

- Look at how lead gets into your body
- Toxic effects of lead
- Safe blood lead levels
- My take home advice

# How does it get in the body

- Through the lungs
  - Inhaling particles <1mcm
- Through the gastrointestinal tract
  - Children can absorb up to 50% compared to adults 20%
  - Iron, zinc deficiency increases absorption
  - High calcium diets reduce absorption

# Where does it go to in the body

- Binds to the red blood cells
- Travels around the body
- Deposited in
  - Bone & teeth
  - Brain
  - Liver and spleen
  - Lung and kidney
- Crosses the placenta to fetus

# How does it get out of the body

- Excreted by the kidneys (65%) & bile (35%)
  - Vitamin C may enhance excretion
- Miniscule amount in hair

# Who is at risk from lead

- Children - especially under 4
- Pregnant women - unborn baby
- Breast feeding mothers
- Those working with lead

# What test do we do?

- Measure of body lead load
- **Blood lead level** used as primary biomarker
  - Urine is insensitive
  - Hair is unreliable
  - Shed teeth is used in research

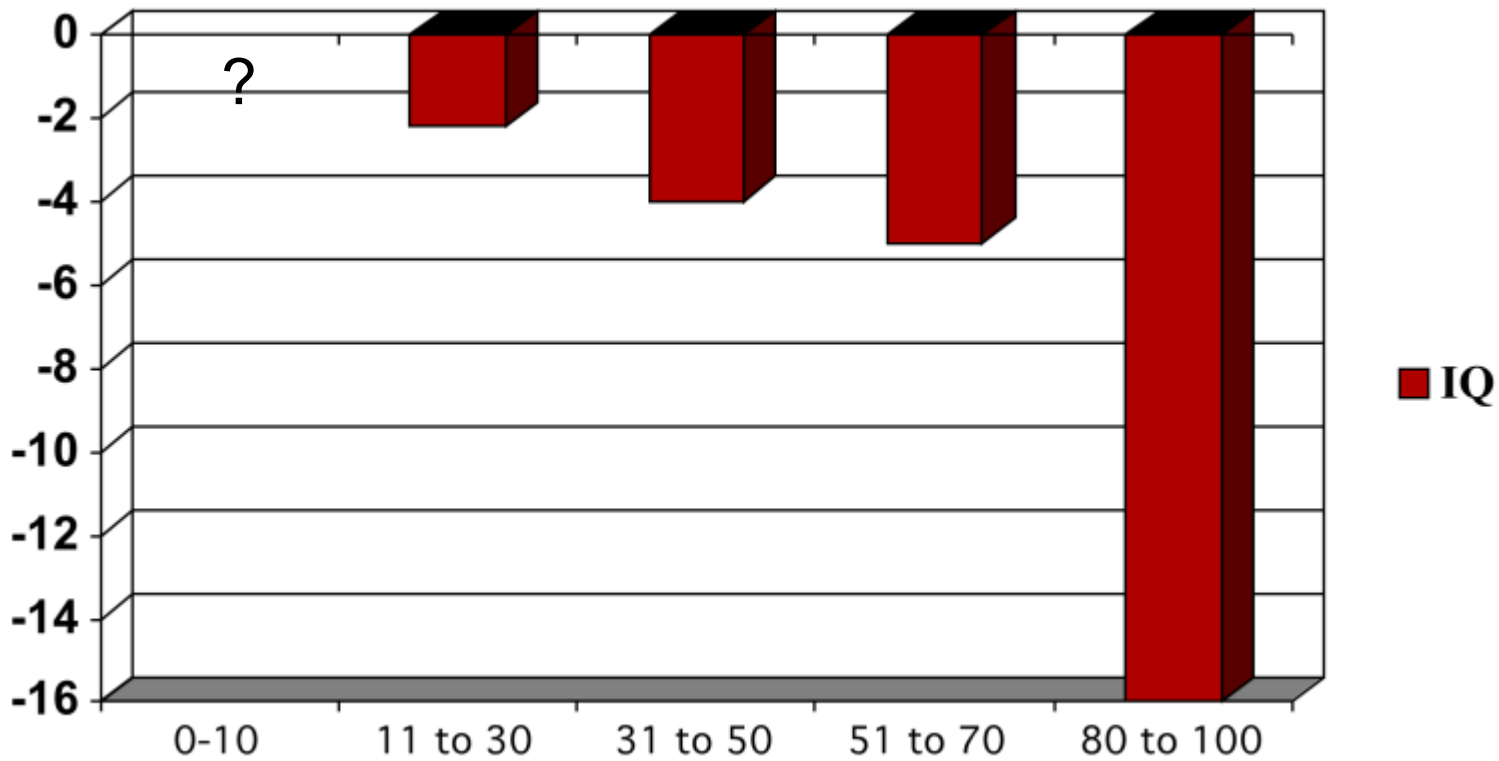
# Toxicity of lead in humans

- Relates to BLL
- Effects organs where lead is deposited



<b>BLL (mcg/dL)</b>	<b>Effect in adults</b>
100	Life threatening encephalopathy
80	Anaemia Impaired kidney function
60	Reduced fertility females
40	Impaired conduction peripheral nerves
30	Hypertension Reduced testicular function

# Relationship between BLL and neurocognitive impairment



Goldfrank's Clinical Toxicology 7th ED

Blood lead level (mcg/dL)

# Many factors influence cognitive development in children

- Genetic
- Prenatal factors
- Socioeconomic factors
- Nutrition
- Smoking/drugs
- Parent and family nurturing

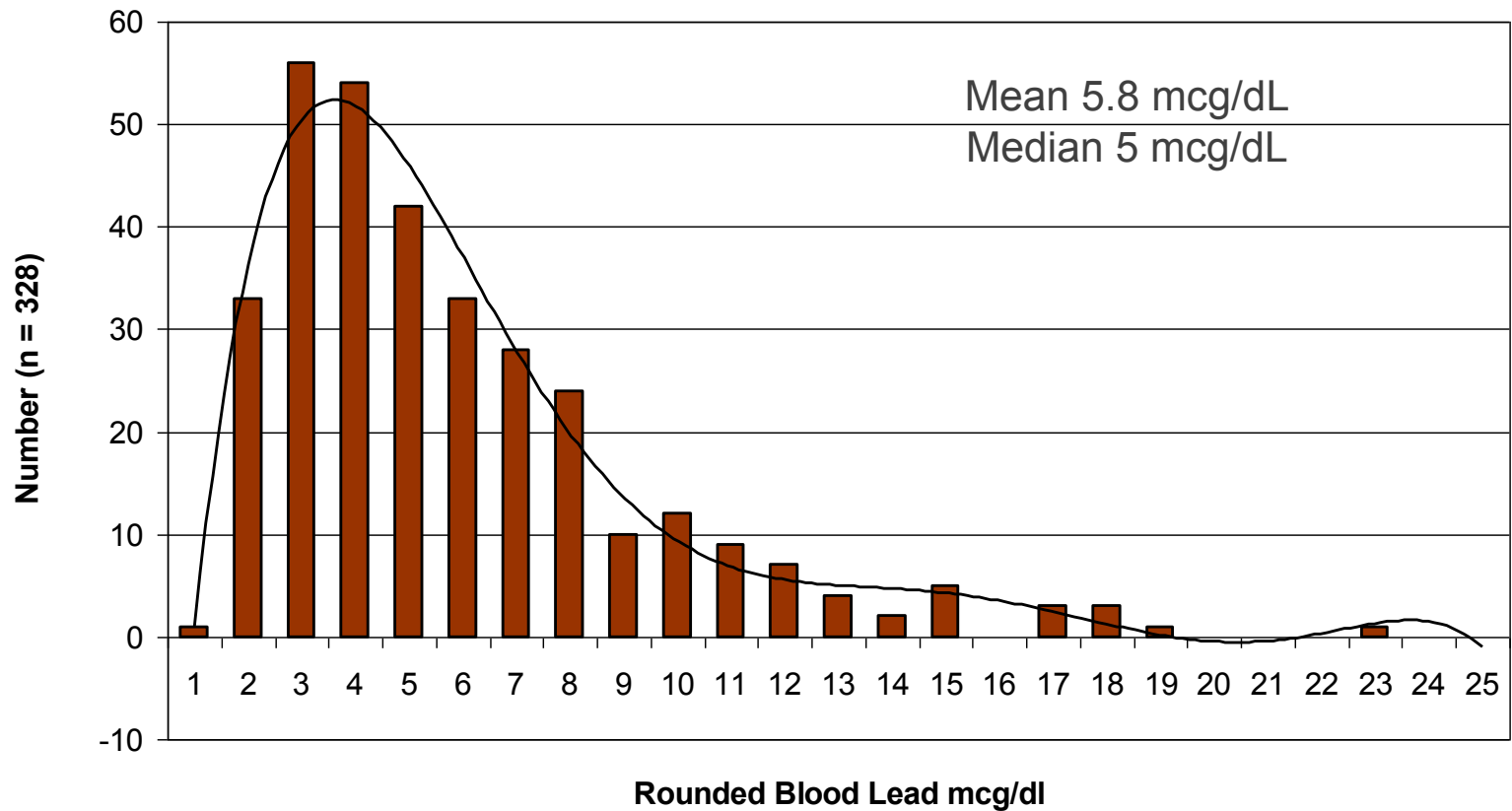
# What is a the current 'level of concern' recommended BLL for children?

- Great debate
- NHMRC, CDC, American Academy of Paediatrics, WHO
  - $BLL > 10 \text{mcg/dL}$

# What is a the current 'safe' recommended BLL for children

- “no effective clinical or public health intervention identified that reliably reduces BLL if  $<10\text{mcg/dL}$ ”
- “No one threshold for adverse events has been identified”
- Aim to have BLL as low as possible and target those with  $>10\text{mcg/dL}$

### Mt Isa Blood Lead Survey July 2007: children 1 - 4 years



# Variation in BLL with age

<b>Age</b>	<b>Mean BLL mcg/dL</b>
6 months	3.4
24 months	9.7
61 months	5.8

Canfield et al NEJM 03



# Controversies





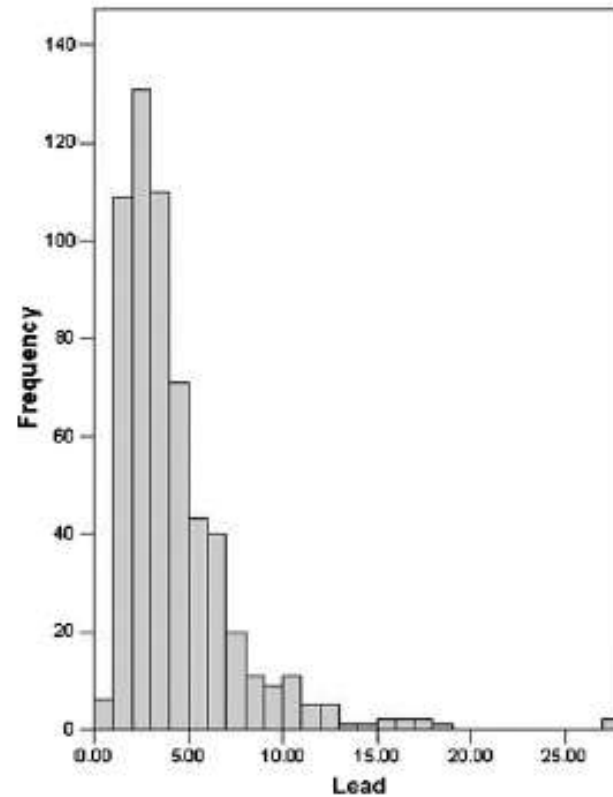
Effects of early childhood lead exposure on academic performance and  
behaviour of school aged children *Arch Dis Child* 2009

- 582 children at 30 months had BLL
- Developmental, behavioural and standardised educational outcomes at 7 - 8 yrs
- UK study

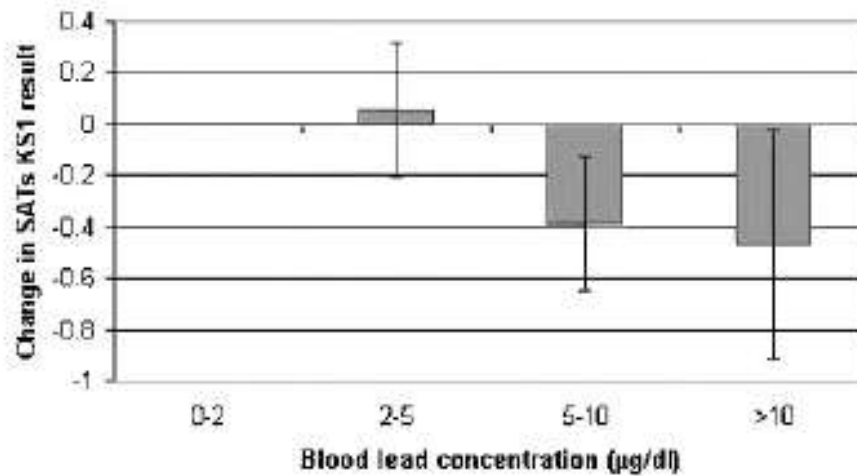
# Results

- 488 cases had all data on confounders
- Regression analysis

# Distribution of BLL



**Figure 1** Distribution of lead levels (n = 582). Mean (SD) 4.22 (3.12) µg/dl; 0-2 µg/dl = 21%; 2-5 µg/dl = 52%; 5-10 µg/dl = 21%; >10 µg/dl = 6%.



**Figure 3** Effect of blood lead concentration on writing. KS1, Key Stage 1.

**Table 2** Regression analysis of the effect of blood lead levels on behaviour, attention, co-ordination and school performance outcomes, adjusted for eight confounders

	Linear log lead concentration		Categorical: 2–5 µg/dl		Categorical: 5–10 µg/dl		Categorical: >10 µg/dl	
	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value
<b>SDQ</b>								
Teacher- hyperactivity	1.41 (0.95 to 2.08)	0.09	0.84 (0.47 to 1.52)	0.566	1.25 (0.67 to 2.33)	0.486	2.82 (1.08 to 7.35)	0.034
Teacher- total difficulties	1.29 (0.87 to 1.90)	0.20	1.02 (0.58 to 1.79)	0.957	1.30 (0.71 to 2.37)	0.394	2.69 (1.06 to 6.81)	0.037
Parent- hyperactivity	1.20 (0.91 to 1.58)	0.19	0.88 (0.57 to 1.34)	0.540	1.24 (0.79 to 1.97)	0.350	1.30 (0.62 to 2.71)	0.484
Parent- total difficulties	1.13 (0.85 to 1.48)	0.40	1.13 (0.74 to 1.72)	0.569	1.27 (0.81 to 2.01)	0.299	1.20 (0.57 to 2.51)	0.636
<b>DAWBA</b>								
Activity score	1.11 (0.83 to 1.48)	0.48	0.81 (0.50 to 1.29)	0.369	1.24 (0.77 to 2.01)	0.369	0.96 (0.44 to 2.10)	0.912
Attention score	1.13 (0.84 to 1.51)	0.42	0.83 (0.52 to 1.32)	0.427	1.28 (0.79 to 2.06)	0.323	1.15 (0.54 to 2.47)	0.713
<b>Behaviour</b>								
Anti-social activities	1.54 (1.01 to 2.33)	0.04	0.93 (0.47 to 1.83)	0.833	1.44 (0.73 to 2.84)	0.289	2.90 (1.05 to 8.03)	0.040
<b>Attention</b>								
Selective attention	1.01 (0.76 to 1.34)	0.94	1.03 (0.66 to 1.61)	0.907	0.99 (0.62 to 1.57)	0.958	1.14 (0.54 to 2.40)	0.723
Dual attention	0.92 (0.66 to 1.31)	0.66	1.13 (0.66 to 1.91)	0.662	1.22 (0.70 to 2.14)	0.489	0.48 (0.20 to 1.13)	0.094
Same worlds	1.26 (0.94 to 1.68)	0.12	0.99 (0.64 to 1.53)	0.947	1.31 (0.82 to 2.08)	0.262	1.48 (0.69 to 3.15)	0.311
Opposite worlds	1.18 (0.88 to 1.57)	0.26	1.29 (0.83 to 2.01)	0.249	1.26 (0.79 to 2.03)	0.334	1.04 (0.49 to 2.21)	0.918
<b>SATs</b>								
Reading	0.64 (0.47 to 0.86)	0.004	0.88 (0.54 to 1.43)	0.608	0.51 (0.32 to 0.82)	0.006	0.62 (0.28 to 1.35)	0.226
Writing	0.61 (0.46 to 0.82)	0.001	1.08 (0.69 to 1.71)	0.729	0.49 (0.31 to 0.78)	0.003	0.44 (0.21 to 0.93)	0.031
Spelling	0.55 (0.36 to 0.83)	0.004	1.41 (0.78 to 2.53)	0.252	0.76 (0.40 to 1.42)	0.383		
Mathematics	0.75 (0.56 to 1.00)	0.053	1.38 (0.86 to 2.20)	0.177	0.73 (0.46 to 1.15)	0.171	0.86 (0.41 to 1.81)	0.694

DAWBA, Development And Well-being Assessment; SATs, Standard Assessment Tests; SDQ, Strengths and Difficulties Questionnaire. Reference group 0–2 µg/dl.

# Study conclusions

- Exposure to lead early in childhood even at low levels is harmful on behaviour and school performance
- Reduce level of concern to 5 mcg/dL

AN INFORMATION PAPER FOR PRACTITIONERS AND POLICY MAKERS

## Blood lead levels for Australians

### Introduction

Lead is a heavy metal used extensively in the manufacture of storage batteries, various alloys including solder and ammunition, some plastics and protective coatings. It is not required for human health, and even small amounts of lead and lead compounds can be toxic when ingested or inhaled.

Based on the research evidence on the effects of low-level exposure to lead, it is not possible to make a definitive statement on what constitutes a 'safe level' or level of concern for blood lead concentrations. Bearing this in mind, this Information Paper examines the evidence on the effects of lead exposure and makes recommendations on what should be aimed for in terms of blood lead concentrations in Australia.

### How humans are exposed to lead

Although lead occurs naturally in the environment, human activities have increased levels of lead in the

#### RECOMMENDATIONS

- All Australians should have a blood lead level below 10 µg/dL (micrograms per decilitre).<sup>1</sup>
- All children's exposure to lead should be minimised.
- All women are advised to minimise their exposure to lead both before and during pregnancy and also while breastfeeding.

This Information Paper is intended for health care practitioners and policy makers. It provides background to lead exposure and articulates goals and recommendations for Australia.

The use of lead compounds in petrol, a practice which has ceased in Australia (except under special license). Lead also enters the environment as a consequence of the mining and refining of lead, and other lead manufacturing activities.



**AMERICAN ACADEMY OF PEDIATRICS**  
**POLICY STATEMENT**  
*Organizational Principles to Guide and Refine the AAP Health Care System and/or Improve the Health of All Children*  
**Committee on Environmental Health**

**Lead Exposure in Children: Prevention, Detection, and Management**

**ABSTRACT.** *Recent lead abatement efforts have displaced and blood lead concentrations have dropped in US children, but approximately 20% still live in housing with deteriorated lead-based paint and are at risk of lead exposure with existing regulatory limitations and other environmental limitations combined to suggest that consistently elevated blood lead concentrations, most have less than 10 µg/dL, may beget attention, and there is no threshold yet identified for only effect. Most US children are at significant risk that they would have their blood lead concentrations elevated to lead levels. There is now evidence-based guidance available for managing children with elevated blood lead exposure. Evidence-based information and reports are being prepared to assist states. The focus is on lead-based lead poisoning policy, however, should shift from one identification and management to primary prevention, with a goal of safe housing for all children. Pediatricians are urged to take lead-related environmental, children's exposure, secondary exposure, clinical advice, housing, prevention, behavior.*

**INTRODUCTION.** *The CDC, Center for Disease Control and Prevention (CDC) and the American Academy of Pediatrics (AAP) recommend that all US children have their blood lead concentrations measured at once, 1 year, 2 years of age, when concentrations between and above peak. By 2007, the median blood lead concentration in the United States had decreased and decreased in some cases with never having lived up low cases of elevated blood lead concentrations. The CDC and AAP then began to recommend screening only those children with a greater chance of having an elevated blood lead concentration—those in older housing, those who had a sibling or playmate with an elevated blood lead concentration, or those who had lived in or visited a structure that might contain deteriorating, damaged, or recently resurfaced lead-painted surfaces. Screening of all chil-*

*dren available for Medicaid, among whom were found 87% of those with increased blood lead concentrations,<sup>2</sup> continued to be recommended and had been required by Health Care Financing Administration (HCFA) since the Centers for Medicare and Medicaid Services regulations since 1995.*

*This new policy statement replaces the 2000 statement and includes discussion of new data, including:*

- Reliable estimation of the percentage of the US house containing lead-based paint.
- Results from a large clinical trial showing that children in children with severely elevated blood lead concentrations does not improve cognitive or neuropsychologic test scores.<sup>3</sup>
- Documentation of uncertainty in assessing severe versus clinically significant children.<sup>4</sup>
- Further confirmation of the link between lead exposure in early childhood and subsequent behavior for starting school.<sup>5,6</sup> and
- New data showing inverse associations between blood lead concentrations less than 10 µg/dL and IQ.<sup>7,8</sup>

*The lead approach to lead poisoning is to prevent exposure in the first place, but it will be years before that goal is reached. In the meantime, case finding, case management, and prevention of additional exposure will still be required. This document considers relevant aspects of the epidemiology, clinical toxicology, prevention, and treatment of lead exposure in young children and provides recommendations for pediatricians as well as public health authorities.*

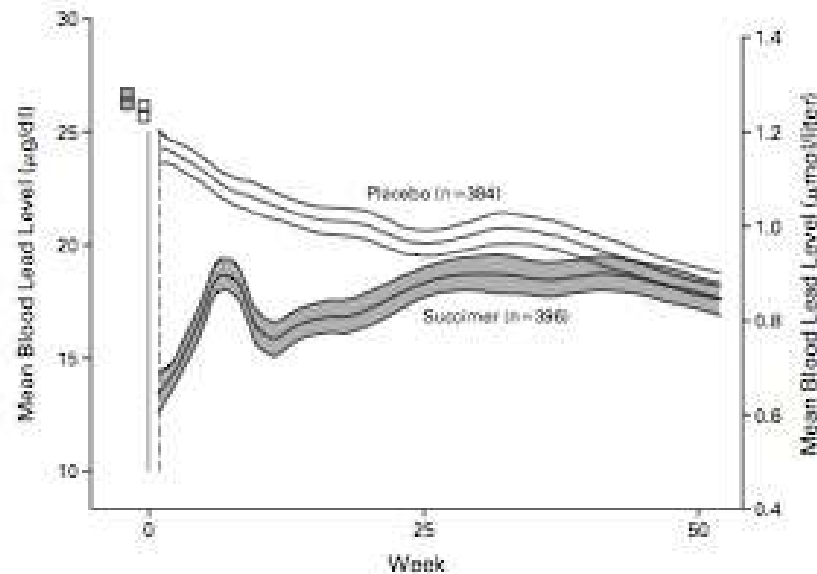
**DECLINE OF LEAD POISONING IN THE UNITED STATES**

*Lead is an element and occurs naturally, but blood lead concentrations are quite low in the absence of industrial activities.<sup>9</sup> In the United States, there were historically 2 major sources of lead: naturally derived lead for children (dust, soil), mostly from the occupational of gasoline containing tetraethyl lead and leaded pipe and steel, mostly from deteriorating lead paint. Both contribute to soil lead. A steady decline in exposure to airborne lead in the United States has occurred since 1980. Federal legislation in the 1970s removed lead from gasoline and decreased automobile emissions from smelters and other sources, causing blood lead concentrations in children to decrease. From 1996 to 2001, studies that sampled lead in their full office, US children 1 to 5 years*

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 WWW.PEDIATRICS.VOL. 124 No. 2 August 2009

# Antidote: Succimer = 2,3dimercaptosuccinic acid [DMSA]

The New England Journal of Medicine



**Figure 1.** Mean Blood Lead Levels and 95 Percent Pointwise Confidence Intervals at Base Line and after the Initiation of Treatment in Children in the Succimer and Placebo Groups.

The squares in the upper left are the base-line values, which were measured about nine days before treatment was initiated (shaded squares indicate the succimer group, and open squares the placebo group). Means for the curves were calculated by locally weighted regression. The broken vertical line marks one week after randomization, which is the first time blood lead levels were measured after the initiation of treatment. (Adapted from the Treatment of Lead-Exposed Children Trial Group<sup>13</sup> with the permission of the publisher.)

Rogan NEJM 2001





# Household interventions






## Household interventions for prevention of domestic lead exposure in children (Review)

Yech B, Woolfenden S, Wheeler DM, Alperstein G, Leaphor B



This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2009, Issue 1

<http://www.thecochranelibrary.com>

- 
- To determine the effectiveness of household interventions in reducing lead exposure
  - 12 studies
  - All in the USA

# Conclusion

- No evidence of effectiveness for household interventions for education or dust controls
- Insufficient evidence for soil abatement
- Further trials required to establish the most effective intervention for the prevention of lead exposure

# Toxicologist take home points

- Lead is here in Mt Isa
- Children absorb more lead than adults
- Children around 2 years seem to have the highest BLL
- Children probably absorb most of the lead through ingestion

# Know the potential sources of lead

- Dust
- Lead paint and home renovations
- Contaminated people, clothes cars or items
- Rain water

# Reduce the exposure

- Wash hands (especially children) before eating
- Wet wipe and mop
- Those working with lead shower and change before coming home
- Shoes/work gear outside
- Reduce exposure to potentially contaminated soil

# Diet

- Regular meals
- Diet high in iron, zinc, calcium and vit C



# Positive family

- Positive family & child psychosocial experience has significant effect on children's cognitive development

# Blood lead levels

- Aim for BLL < 10 mcg/dL
  - The lower the better
- **Everyone** should be tested
- Opportunity to explain lead and its toxicity/reduction of exposure

# If BLL > 10 mcg/dL

Chapter 3. Medical Assessment and Interventions

Table 3.1. Summary of Recommendations for Children with Confirmed (Venous) Elevated Blood Lead Levels

Blood Lead Level (µg/dL)				
10-14	15-19	20-44	45-69	≥70
<ul style="list-style-type: none"> <li>• Lead education                             <ul style="list-style-type: none"> <li>– Dietary</li> <li>– Environmental</li> </ul> </li> <li>• Follow-up blood lead monitoring</li> </ul>	<ul style="list-style-type: none"> <li>• Lead education                             <ul style="list-style-type: none"> <li>– Dietary</li> <li>– Environmental</li> </ul> </li> <li>• Follow-up blood lead monitoring</li> <li>• Proceed according to actions for 20-44 µg/dL if:                             <ul style="list-style-type: none"> <li>– A follow-up BLL is in this range at least 3 months after initial venous test</li> </ul> </li> <li>or</li> <li>– BLLs increase</li> </ul>	<ul style="list-style-type: none"> <li>• Lead education                             <ul style="list-style-type: none"> <li>– Dietary</li> <li>– Environmental</li> </ul> </li> <li>• Follow-up blood lead monitoring and physical exam</li> <li>• Lab work:                             <ul style="list-style-type: none"> <li>– Hemoglobin or hematocrit</li> <li>– Iron status</li> </ul> </li> <li>• Environmental investigation</li> <li>• Lead hazard reduction</li> <li>• Neurodevelopmental monitoring</li> <li>• Abdominal X-ray (if particulate lead ingestion is suspected) with bowel decontamination if indicated</li> </ul>	<ul style="list-style-type: none"> <li>• Lead education                             <ul style="list-style-type: none"> <li>– Dietary</li> <li>– Environmental</li> </ul> </li> <li>• Follow-up blood lead monitoring and physical exam</li> <li>• Complete history and physical exam</li> <li>• Complete neurological exam</li> <li>• Lab work: Hemoglobin or hematocrit                             <ul style="list-style-type: none"> <li>– Iron status</li> <li>– FEP or ZPP</li> </ul> </li> <li>• Environmental investigation                             <ul style="list-style-type: none"> <li>• Lead hazard reduction</li> <li>• Neurodevelopmental monitoring</li> <li>• Abdominal X-ray with bowel decontamination if indicated</li> <li>• Chelation therapy</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Hospitalize and commence chelation therapy</li> <li>• Proceed according to actions for 45-69 µg/dL</li> </ul>
<p>The following actions are NOT recommended at any blood lead level:</p> <ul style="list-style-type: none"> <li>• Searching for gingival lead lines</li> <li>• Testing of neurophysiologic function</li> <li>• Evaluation of renal function (except during chelation with EDTA)</li> <li>• Testing of hair, teeth, or fingernails for lead</li> <li>• Radiographic imaging of long bones</li> <li>• X-ray fluorescence of long bones</li> </ul>				

- Test entire family
- Involve Public Health Unit

# Summary of medical management

- BLL is best measure of lead body load
- $BLL < 45 \text{ mcg/dL}$ 
  - Not use chelating drug
  - Seek environmental source and limit
- Asymptomatic child  $BLL > 45 \text{ mcg/dL}$ 
  - Seek source
  - Chelate with succimer dw toxicologist/PIC
- Symptomatic or  $BLL > 70 \text{ mcg/dL}$ 
  - Admit
  - Immediate chelate - dw Toxicologist/PIC

# Conclusion

- Elevated BLL indicates environmental contamination
- Main concern is in children and the risk of cognitive development
- Major management [BLL < 45 mcg/dL] is identifying the lead source and reducing the exposure

# Mt Isa

- Will have an ongoing lead exposure
- Need to have an ongoing process of education of community to reduce exposure to children
- Need to test the entire population