
Lead - from a toxicologist's perspective

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Aim

- ▣ Look at how lead gets into your body
- ▣ Toxic effects of lead
- ▣ BLL level of concern
- ▣ Controversies
- ▣ My take home advice

How does it get in the body

- ▣ Through the lungs
 - ▣ Inhaling particles <1 mcm

- ▣ 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

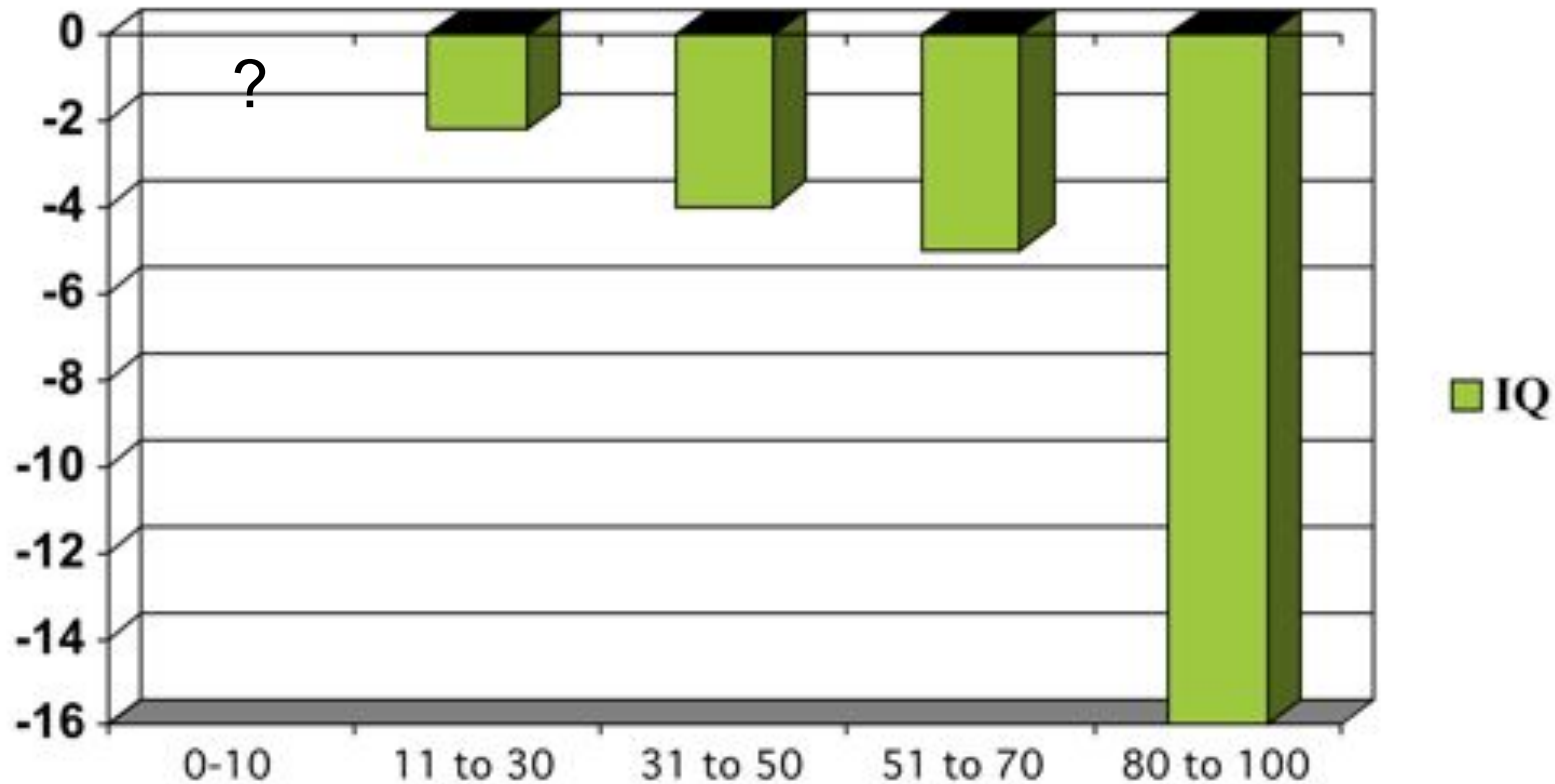
Toxicity of lead in humans

- ▣ Relates to BLL
- ▣ Effects organs where lead is deposited

BLL (mcg/dL)	Effect in adults
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



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>10mcg/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 $>10\text{mcg/dL}$
- Advisory Committee for Childhood Lead Poisoning Prevention (CDC) recommends acting on $\text{BLL} > 5\text{mcg/dL}$

Variation in BLL with age

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

Table 7. Summary of geometric mean blood lead levels by sex, Indigenous status and age for the 2007 and 2010 surveys

	2010		2007	
	Number	Geometric mean blood lead level (95% confidence intervals)	Number	Geometric mean blood lead level (95% confidence intervals)
All*	167	4.27 (3.96, 4.61)	400	4.97 (4.69, 5.24)
Indigenous status				
Indigenous*	37	5.44 (4.53, 6.53)	83	7.05 (6.25, 7.95)
Non Indigenous*	130	3.98 (3.68, 4.32)	315	4.54 (4.28, 4.82)
Sex				
Male*	92	4.17 (3.79, 4.58)	214	5.13 (4.75, 5.52)
Female	75	4.39 (3.88, 4.98)	184	4.77 (4.39, 5.18)
Age (years)				
12-23 months (1 year)	49	4.35 (3.82, 4.96)	84	5.39 (4.80, 6.07)
24-35 months (2 years)	59	4.72 (4.15, 5.37)	114	5.50 (4.93, 6.14)
36-47 months (3 years)	30	3.85 (3.10, 4.77)	106	4.48 (4.01, 4.99)
48-59 months (4 years)	23	3.75 (3.14, 4.49)	95	4.56 (4.11, 5.06)

* Comparison of 2010 and 2007 results was statistically significant ($p \leq 0.05$)

Table 8. Numbers and percentages of children with elevated blood lead levels $\geq 10\mu\text{g}/\text{dl}$ by Indigenous status, sex and age group

	2010		2007	
	Number	Percentage	Number	Percentage
All*	8	4.8	45	11.3
Indigenous status				
Indigenous*	3	8.1	22	26.5
Non Indigenous	5	3.9	23	7.3
Sex				
Male*	4	4.4	26	12.1
Female	4	5.3	18	9.8
Age (years)				
12-23 months (1 year)	2	4.1	9	10.7
24-35 months (2 years)	3	5.1	19	16.7
36-47 months (3 years)	2	6.7	9	8.5
48-59 months (4 years)	1	3.5	8	8.4

* Comparison of 2010 with 2007 results was statistically significant ($p \leq 0.05$)

Controversies



Blood lead levels <5mcg/dL



**Low Level Lead Exposure Harms Children: A Renewed Call for
Primary Prevention**

Report of the

Advisory Committee on Childhood Lead Poisoning Prevention

of the Centers for Disease Control and Prevention

January 4, 2012

Disclaimer

This document was solely produced by the Advisory Committee for Childhood Lead Poisoning Prevention. The posting of this document to our website in no way authorizes approval or adoption of the recommendations by CDC. Following the committee vote on January 4, 2012 to approve these recommendations, HHS and CDC will begin an internal review process to determine whether to accept all or some of the recommendations and how to implement any accepted recommendations.

Recommends

- ▣ Acknowledges that there is no safe threshold for lead
- ▣ Remove term “level of concern”
- ▣ Monitor children and investigate source if BLL > 5mcg/dL
 - ▣ Assess children for iron deficiency & nutritional status
 - ▣ Aim for primary prevention of lead exposure
 - ▣ Environmental screening
- ▣ Communication of BLL results

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

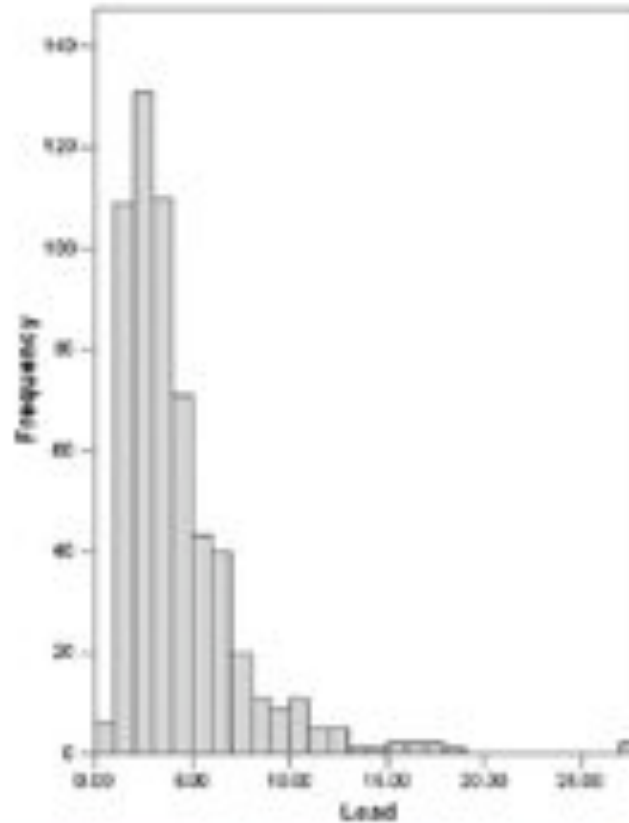


Figure 1 Distribution of lead levels (n = 582). Mean (SD) 4.22 (3.12) $\mu\text{g/dl}$; 0-2 $\mu\text{g/dl}$ = 21%; 2-5 $\mu\text{g/dl}$ = 52%; 5-10 $\mu\text{g/dl}$ = 21%; >10 $\mu\text{g/dl}$ = 6%.

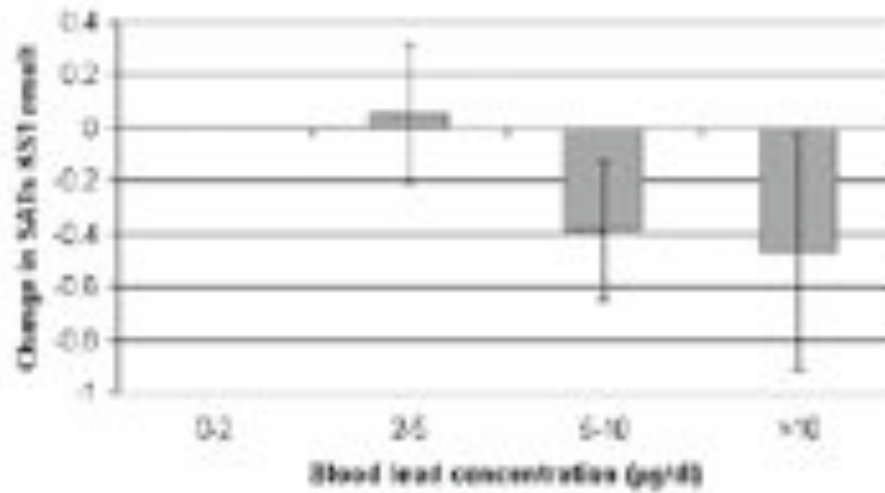


Figure 3 Effect of blood lead concentration on writing, KS1, Key Stage 1.

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

Other issues

- BLL from 5 mg/dL to 10 mcg/dL
- IQ may drop by ~ 2 - 3 pts Canfield NEJM 03
- Increase in hyperactivity by 0.3pts Chandramouli 09
- Reduction in writing score by 0.4pts Chandramouli 09

Many factors influence cognitive development in children

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

INFORMATION PAPER AUGUST 2009

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 strived 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

The use of lead compounds in paint, a practice which has ceased in Australia (except under special licence), lead also enters the environment as a consequence of the mining and refining of lead, industrial and manufacturing activities

RECOMMENDATIONS

- All Australians should have a blood lead level below 10 µg/dL (micrograms per decilitre)
- 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 attention goals and recommendations for Australia.

Level of concern > 10mcg/dL

AMERICAN ACADEMY OF PEDIATRICS

POLICY STATEMENT

Department of Pediatrics, American Academy of Pediatrics, 505 North Dearborn Street, Elk Grove Village, IL 60007-1098

A COMMITTEE ON ENVIRONMENTAL HEALTH

Lead Exposure in Children: Prevention, Detection, and Management

OBJECTIVE: Lead has neurotoxic effects on children, and blood lead concentrations have increased in the United States. This policy statement provides information on the prevention, detection, and management of lead exposure in children and adults who are exposed to lead.

KEY WORDS: lead, blood lead, neurotoxicity, children, prevention, detection, management

INTRODUCTION: Lead is a toxic heavy metal that is found in many environments. Lead exposure in children is a public health problem because of its neurotoxic effects. The American Academy of Pediatrics (AAP) is committed to the prevention, detection, and management of lead exposure in children and adults who are exposed to lead.

PREVENTION: The AAP recommends that all children under the age of 6 years have a blood lead level (BLL) test. The AAP also recommends that all children under the age of 6 years have a BLL test if they live in a lead-painted house, work in a lead-painted house, or work in a lead-painted house. The AAP also recommends that all children under the age of 6 years have a BLL test if they live in a lead-painted house, work in a lead-painted house, or work in a lead-painted house.

DETECTION: The AAP recommends that all children under the age of 6 years have a BLL test. The AAP also recommends that all children under the age of 6 years have a BLL test if they live in a lead-painted house, work in a lead-painted house, or work in a lead-painted house.

MANAGEMENT: The AAP recommends that all children with a BLL of 10 µg/dL or higher have a BLL test. The AAP also recommends that all children with a BLL of 10 µg/dL or higher have a BLL test. The AAP also recommends that all children with a BLL of 10 µg/dL or higher have a BLL test.

Why not just treat all the kids with
antidote?

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

The New England Journal of Medicine

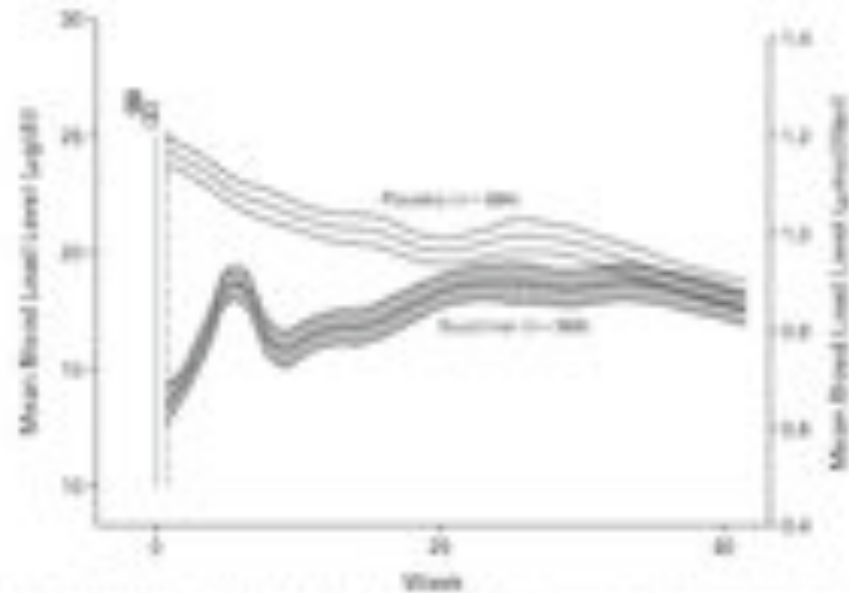


Figure 5. Mean Blood Lead Levels and 95 Percent Prediction Confidence Intervals at Baseline and after the Initiation of Succimer or Placebo in the Succimer and Placebo Groups.
The squares in the upper left are the baseline values, which were measured about one week before treatment was initiated (squares include the succimer group, and upper 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 point lead levels were measured after the initiation of treatment. (Adapted from the Treatment of Lead-Exposed Children: The Group¹ with the permission of the author(s).)

Household interventions



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

Yeoh B, Woolfenden S, Wheeler DM, Alperstein G, Lanphear B



- 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

Australian experience

- ▣ Esperance (WA) lead contamination due to lead transport 2007

- ▣ Instituted
 - ▣ Testing of all children
 - ▣ Nutritional intervention
 - ▣ Cleaning – wet mop, boots outside
 - ▣ Testing water from rainwater tanks and cleaning
 - ▣ Testing soil and removing A Jones 09

Follow-up Blood Lead Levels (BLL) for children* in the Esperance Community carried out in October 2007 are as follows:

Follow-up Blood Lead Levels (BLL) for children* in the Esperance Community Results as at 6th November 2007	
Number of children $\geq 5\mu\text{g/dL}$ on first test	83
Number of children with 3 tests	40 (48%)
Number of children with only 2 tests	27 (33%)
Number of children not retested	16 (19%)
81% of eligible children have had at least one re-test	
Average BLL 1st Test - all children (n=83)	6.8
Average BLL 2nd Test (n=67)	4.1
Average BLL 3rd Test (n=40)	4.1
Number with lower BLL on second test	62 (92.5%)
Number whose BLL dropped between 2nd & 3rd tests	21 (52.5%)
BLL at last test for the 67 children that have had at least one re-test:	
<5 $\mu\text{g/dL}$	51 (76%)
5 $\mu\text{g/dL}$	10 (15%)
6 $\mu\text{g/dL}$	1 (1.5%)
7 $\mu\text{g/dL}$	2 (3%)
8 $\mu\text{g/dL}$	1 (1.5%)
>10 $\mu\text{g/dL}$	2 (3%)

* Children aged less than 5 years with initial BLL 5 or more $\mu\text{g/dL}$.

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What do I recommend?



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
 - Listen for further advice from NHMRC
- **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)				
13-14	15-19	20-44	45-69	≥70
<ul style="list-style-type: none"> Lead education <ul style="list-style-type: none"> Dietary Environmental Follow-up blood lead monitoring 	<ul style="list-style-type: none"> Lead education <ul style="list-style-type: none"> Dietary Environmental Follow-up blood lead monitoring Proceed according to actions for 20-44 µg/dL, if <ul style="list-style-type: none"> A follow-up BLL is in this range at least 3 months after initial venous test BLLs increase 	<ul style="list-style-type: none"> Lead education <ul style="list-style-type: none"> Dietary Environmental Follow-up blood lead monitoring Complete history and physical exam Lab work <ul style="list-style-type: none"> Hemoglobin or hematocrit Iron status Environmental investigation Lead hazard reduction Neurodevelopmental monitoring Abdominal X-ray if peristaltic lead ingestion is suspected with bowel decontamination if indicated 	<ul style="list-style-type: none"> Lead education <ul style="list-style-type: none"> Dietary Environmental Follow-up blood lead monitoring Complete history and physical exam Complete neurological exam Lab work <ul style="list-style-type: none"> Hemoglobin or hematocrit Iron status PEP or ZPP Environmental investigation Lead hazard reduction Neurodevelopmental monitoring Abdominal X-ray with bowel decontamination if indicated Chelation therapy 	<ul style="list-style-type: none"> Hospitalize and commence chelation therapy Proceed according to actions for 45-69 µg/dL
<p>The following actions are NOT recommended at any blood lead level:</p> <ul style="list-style-type: none"> Searching for gingival lead lines Testing of neurophysiologic function Evaluation of renal function (except during chelation with EDTA) Testing of hair, teeth, or fingernails for lead Radiographic imaging of long bones X-ray fluorescence of long bones 				

Managing Elevated Blood Lead Levels Among Young Children

41

- Test entire family
- Involve Public Health Unit

CDC

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



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YOU ARE INVITED TO A PUBLIC INFORMATION SEMINAR ON LIVING SAFELY WITH LEAD

DR MARK LITTLE SEMINAR

The Living with Lead Alliance invite the Mount Isa Community to our PUBLIC INFORMATION SEMINAR

Presented by leading toxicologist Dr Mark Little.

Thursday 3rd May 2012

3.30pm to 5.30pm

Questions?

