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?

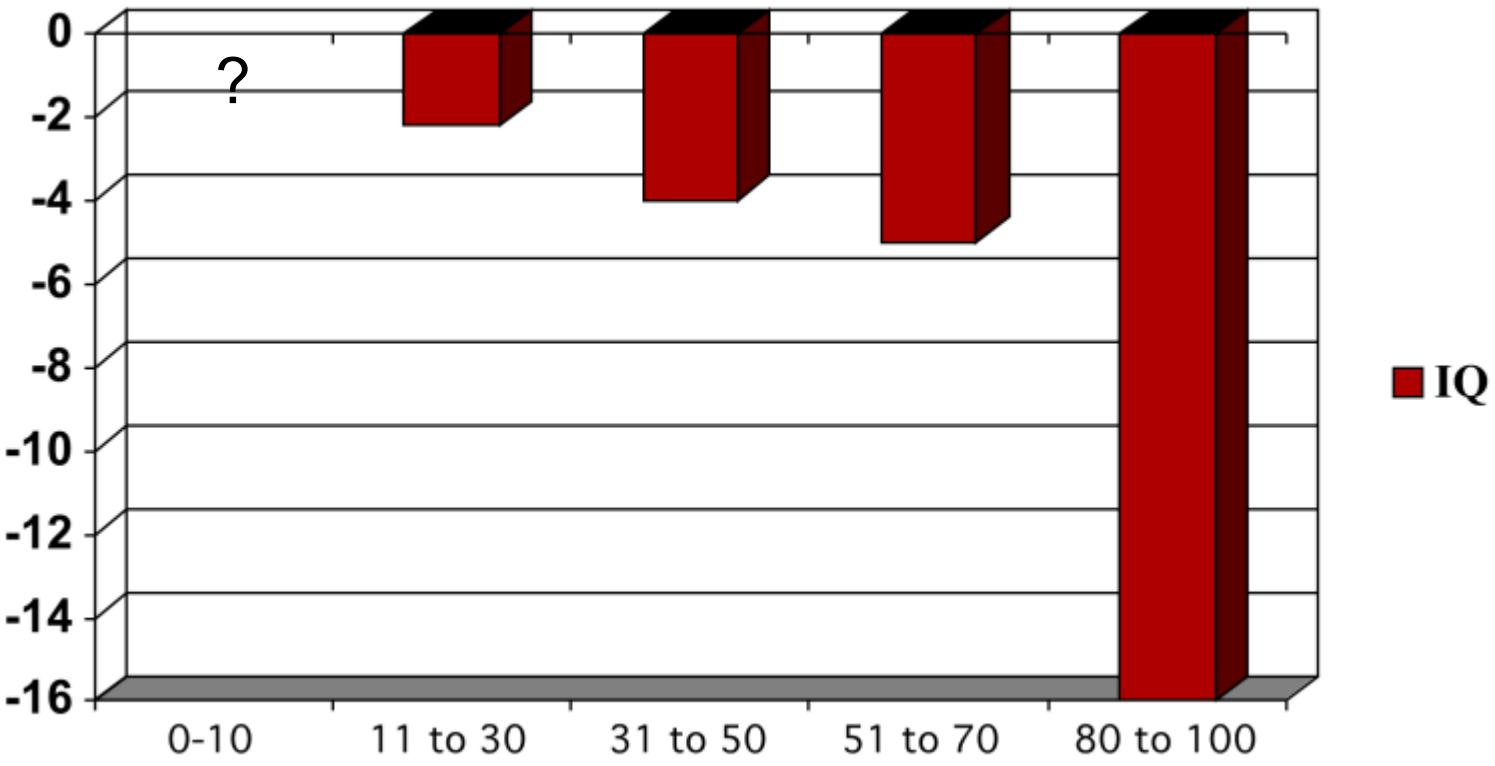
- Measure of body lead load
- **Blood lead level** used as primary biomarker
  - Urine is insensitive
  - Hair in unreliable
  - Shed teeth is used in research

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

Blood lead level (mcg/dL)

Many factors influence cognitive development in children

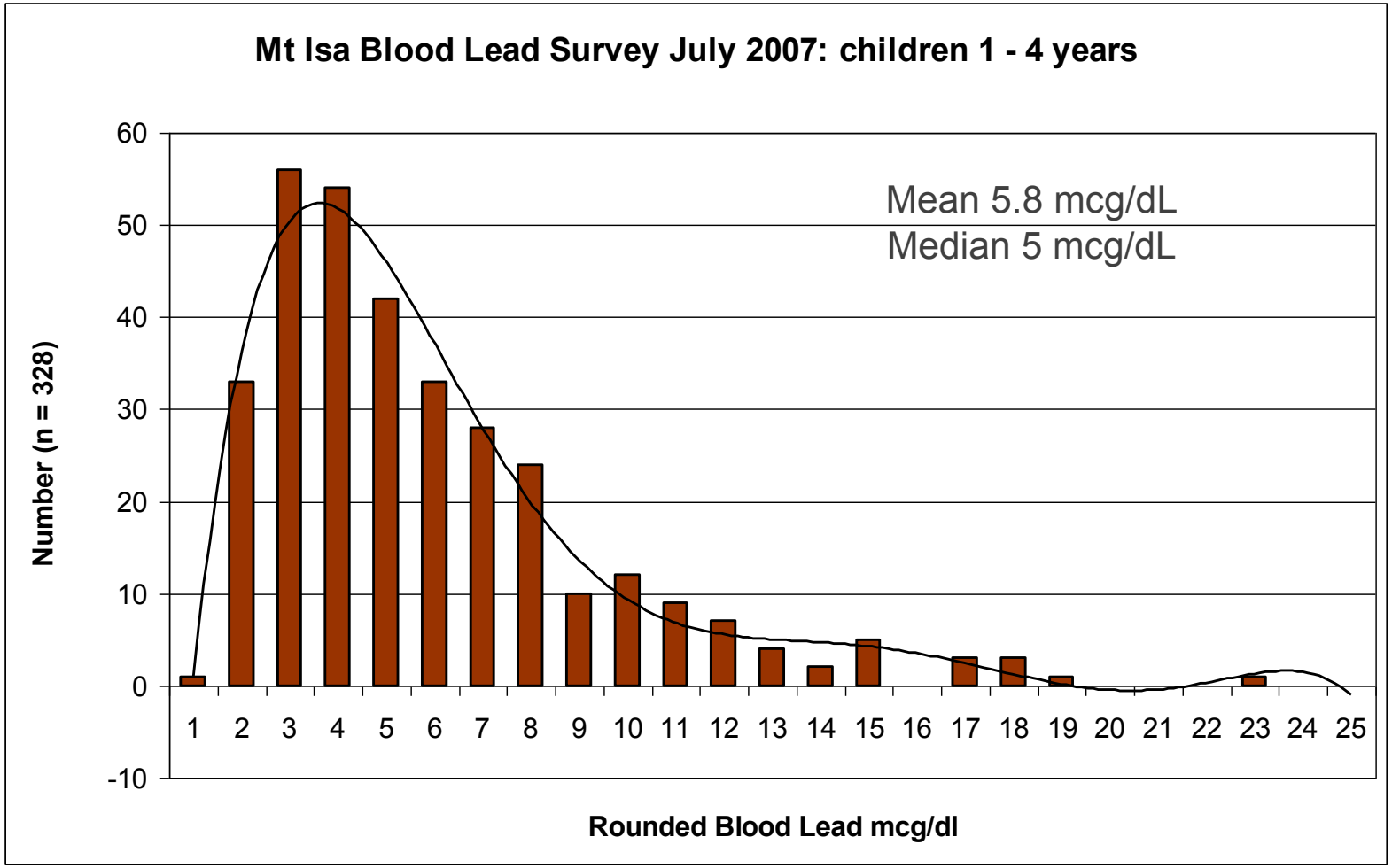
- Genetic
- Prenatal factors
- Socioeconomic factors
- Nutrition
- Smoking/drugs
- Parent and family nuturing

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 <10mcg/dL"
- "No one threshold for adverse events has been identified"
- Aim to have BLL as low as possible and target those with >10mcg/dL


Mt Isa Blood Lead Survey July 2007: children 1 - 4 years
Mean 5.8 mcg/dL
Median 5 mcg/dL
Number (n = 328)
60
50
40
30
20
10
0
-10
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
Rounded Blood Lead mcg/dl

Variation in BLL with age

Age	Mean BLL mcg/dL
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

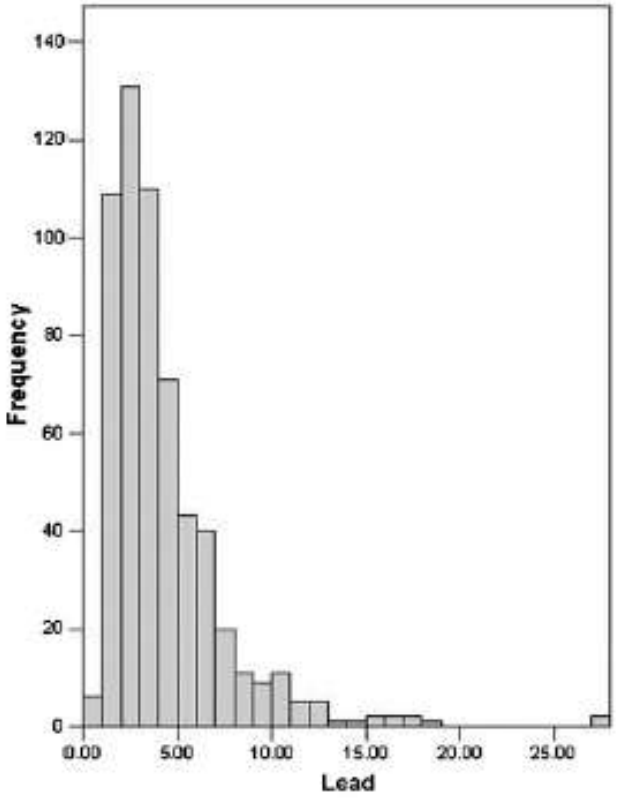


Figure 1 Distribution of lead levels (n = 582). Mean (SD) 4.22 (3.12) µg/dl; 0–2 µg/dl = 21%; 2–5 µg/dl = 52%; 5–10 µg/dl = 21%; >10 µg/dl = 6%.

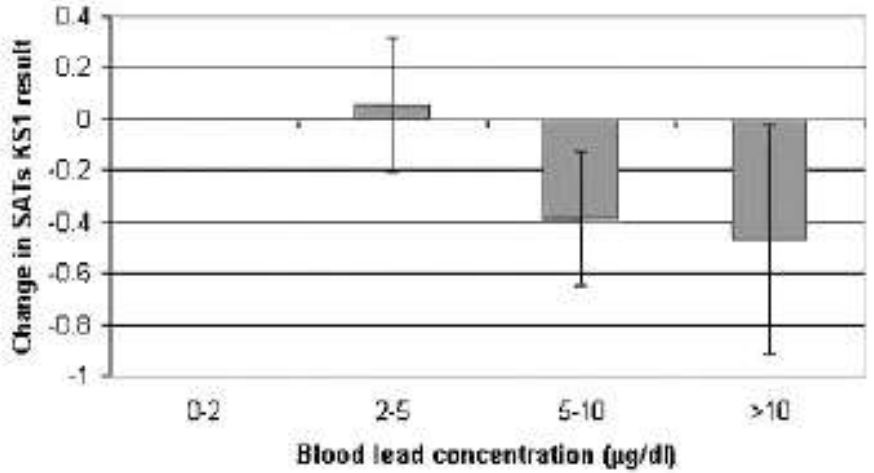


Figure 3 Effect of blood lead concentration on writing. KS1, Key Stage 1.

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
SDQ								
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
DAWBA								
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
Behaviour								
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
Attention								
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
SATs								
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


NHMRC

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.

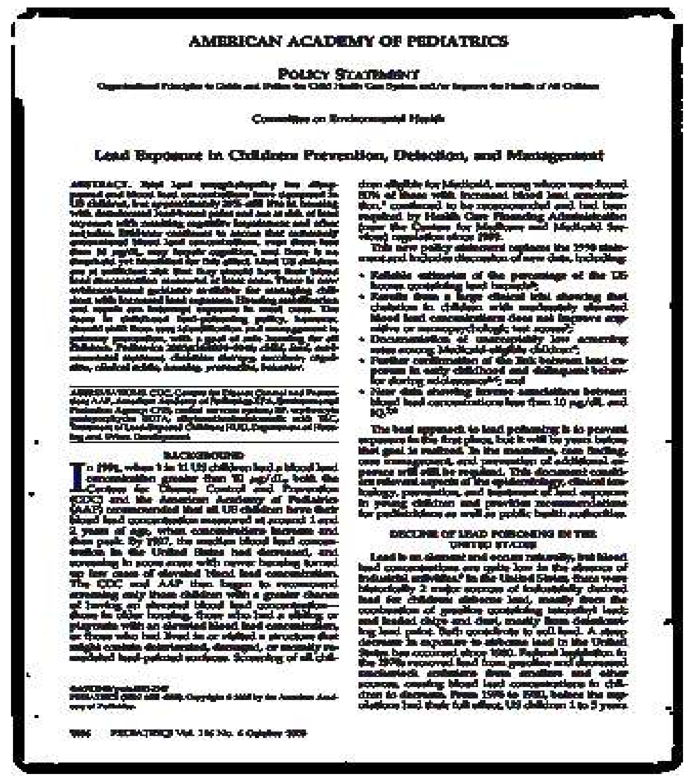
RECOMMENDATIONS

- All Australians should have a blood lead level below 10 µg/dL (micrograms per decilitre).[1]
- 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.

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 petrol, 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


AMERICAN ACADEMY OF PEDIATRICS

POLICY STATEMENT

Committee on Environmental Health

Lead Exposure in Children: Prevention, Detection, and Management

BACKGROUND

DECLINE OF LEAD POISONING IN THE UNITED STATES

PEDIATRICS Vol. 116 No. 4 October 2005

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

The New England Journal of Medicine

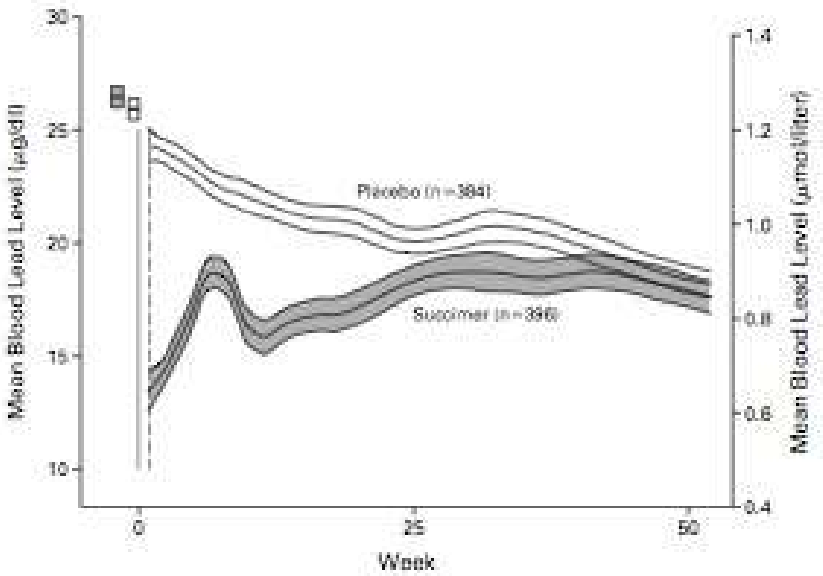


Figure 1. Mean Blood Lead Levels and 95 Percent Pointwise Confidence Intervals at Base Line and after the Initiation of Treatment in Children in the Succimer and Placebo Groups.

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[1] with the permission of the publisher.)

Rogan NEJM 2001

Household interventions

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

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

THE COCHRANE COLLABORATION®

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 effectiness 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 that 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

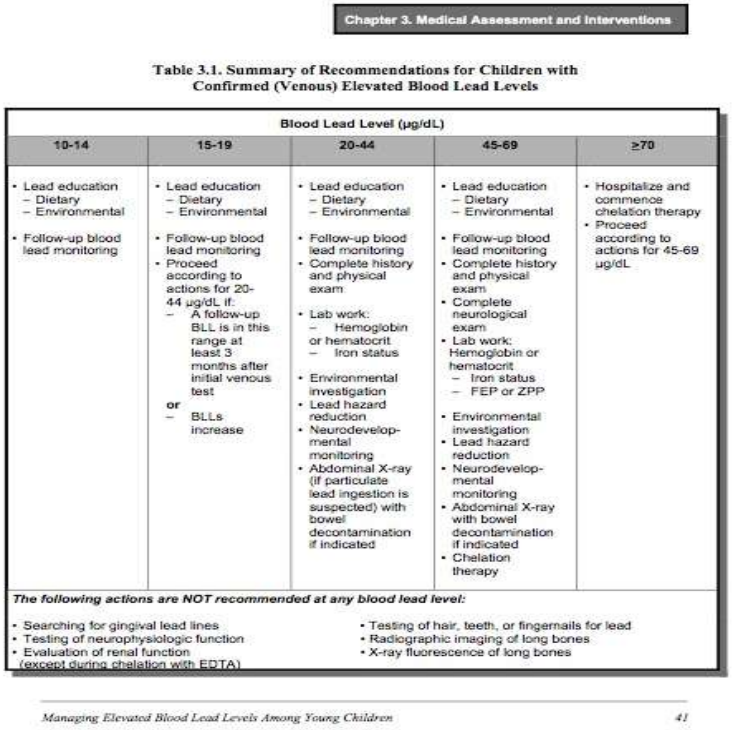
Positive family

- 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**
• Lead education – Dietary – Environmental • Follow-up blood lead monitoring	• Lead education – Dietary – Environmental • Follow-up blood lead monitoring • Proceed according to actions for 20-44 µg/dL if: – A follow-up BLL is in this range at least 3 months after initial venous test or – BLLs increase	• Lead education – Dietary – Environmental • Follow-up blood lead monitoring • Complete history and physical exam • Lab work: – Hemoglobin or hematocrit – Iron status • Environmental investigation • Lead hazard reduction • Neurodevelop-mental monitoring • Abdominal X-ray (if particulate lead ingestion is suspected) with bowel decontamination if indicated	• Lead education – Dietary – Environmental • Follow-up blood lead monitoring • Complete history and physical exam • Complete neurological exam • Lab work: Hemoglobin or hematocrit – Iron status – FEP or ZPP • Environmental investigation • Lead hazard reduction • Neurodevelop-mental monitoring • Abdominal X-ray with bowel decontamination if indicated • Chelation therapy	• Hospitalize and commence chelation therapy • Proceed according to actions for 45-69 µg/dL

The following actions are NOT recommended at any blood lead level:

- 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

CDC

- Test entire family
- Involve Public Health Unit

Summary of medical management

- BLL is best measure of lead body load
- BLL < 45 mcg/dL
  - Not use chelating drug
  - Seek enviromental source and limit
- Asymptomatic child BLL > 45mcg/dL
  - Seek source
  - Chelate with succimer dw toxicologist/PIC
- Symptomatic or BLL > 70 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