Every Tooth Tells A Story

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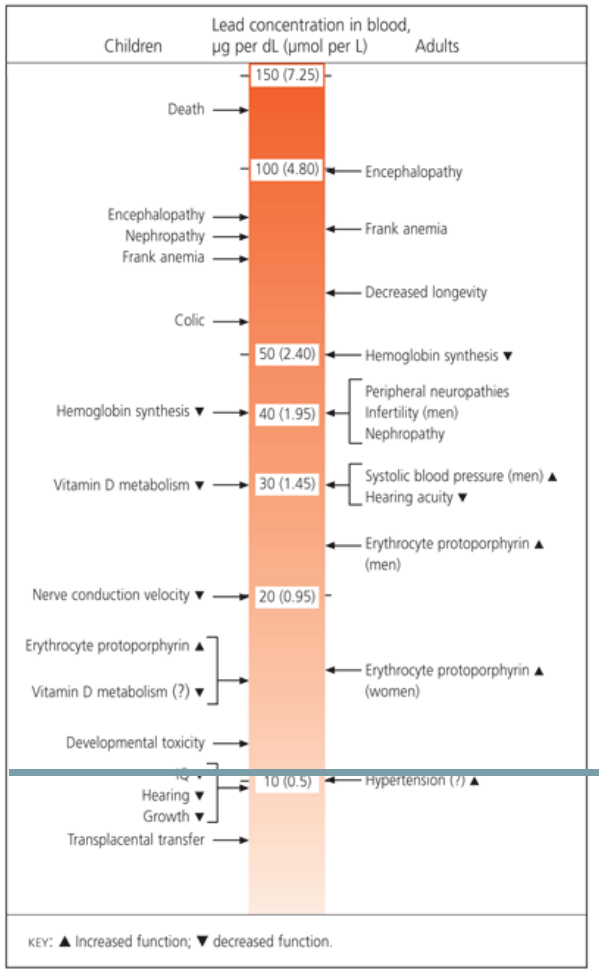
Outline

- Health effects of lead in children
- Biomarkers for measuring exposure
- Shed milk teeth as a biomarker of exposure in longitudinal birth cohort studies

Health effects of lead



- World Health Organisation estimates lead is responsible for:
  - 143,000 deaths per year
  - 0.6% of the global burden of disease worldwide
- Lead toxicity
  - Abdominal cramps (lead colic)
  - Vomiting and anorexia
  - Neurological symptoms: headache, visual disturbance
  - **Blood lead 70µg/dL:** encephalopathy, coma, death
- WHO: blood lead level for action: **10µg/dL**

Lead in human body

- Lead is absorbed through the gut
  - Complex cycling between blood, soft tissue & bone
- Blood
  - Mean half-life of 40 days
- Bone
  - Storage for 10-30 years
  - Bone remodelling leads to release back into blood
  - **Increased remodelling in children and pregnant women**
- Placenta
  - Freely crosses placenta – **fetus vulnerable due to high rates of cell division and differentiation**

Public health measures

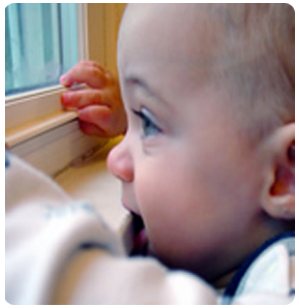
- Public health measures to reduce lead in the UK include:
  - Lead-free paint introduced in 1950s (banned in 1992)
  - Removal of lead from petrol in 1980s (banned in 2000)
  - Reduction of lead in water supply since 1990s

- Secular declines in soil and water lead levels

- No routine measures of lead exposure in children – unclear if these measures are associated with significant reductions in chronic lead exposure

Children remain more vulnerable

- Children are at higher risk of lead exposure and ingestion:
  - Soil: age-related patterns of mouthing, pica
  - Lead paint in older housing: mobile - dust on windowsill
  - Lead pipes in housing
  - Ethnic/cultural exposures: cosmetics, medicines



- Children's lead levels increase from 6-12 months, peak at 18-36 months, then decline
- Older children may have greater cumulative burden

- Inequality: risk is socially patterned
  - Higher lead paint levels in low income housing and schools
  - Lead pipes: formula milk, diluted squash
  - Living near industrially polluted sites and transport hubs
  - Diet: lower calcium

Effect of low level lead exposure on children

- Low level exposures – blood lead level <10µg/dL
  - Exposure during a critical period: developing baby, young child
  - Cumulative and long-term effects

- Adverse effects on pregnancy:
  - Preterm birth and low birth weight
  - Hearing loss
  - May affect boys more than girls

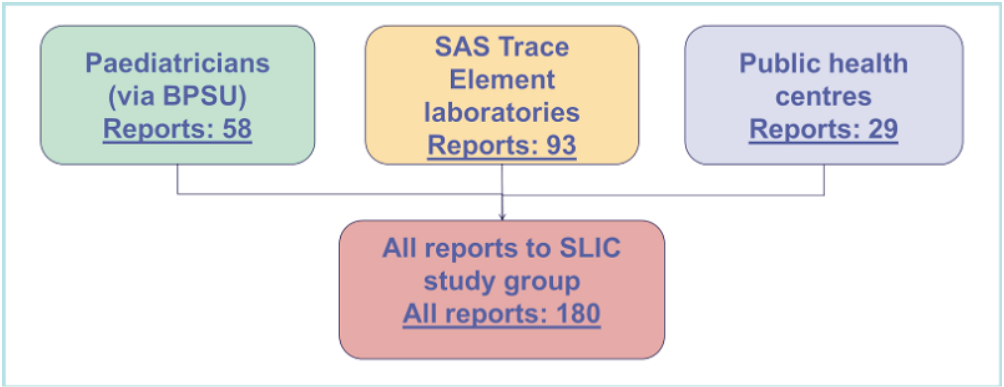
- Adverse effects on young child
  - Poor growth
  - Cognitive and neurodevelopment problems
  - Behaviour problems

SLIC study: Lead toxicity in UK children

- Surveillance of elevated Lead In Children (SLIC) – led by Public Health England
- Incidence of blood lead levels ≥10µg/dL in children aged 16 years and under

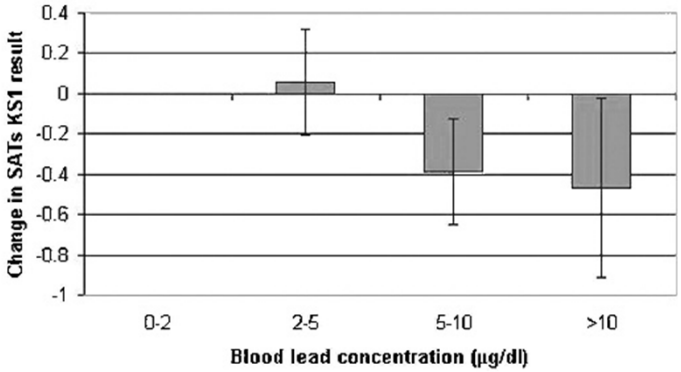
- Cases identified over 24 months from June 2010 until May 2012 through:
  - British Paediatric Surveillance Unit – 3000+ paediatricians
  - Clinical toxicologists
  - Supra-Regional Assay Service (SAS) laboratories
  - Public health centres (e.g. health protection units)

- Source of lead exposure
  - **Lead paint in housing**



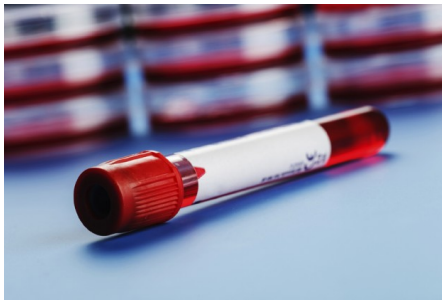
Avon Longitudinal Study of Parents and Children (ALSPAC) – Children of the 90s

- Longitudinal population-based birth cohort study
  - Enrolled >14,000 pregnant women and babies during 1991-1992
- Blood lead study: 488 children
  - Blood samples for lead levels at age 30 months
  - Development, behaviour and school SATs (standardised assessment tests) in reading, writing and spelling at age 7-8 years
- Key findings
  - 6% children had a blood lead level ≥10µg/dL
  - Doubling in blood lead associated with 0.3 point drop in SATs grades
  - Reading/writing scores lower at 5-10µg/dL
  - Antisocial behaviour and hyperactivity increased at >10µg/dL



Measuring lead exposure using blood levels

- Blood
  - Precise, accurate, low-cost, can be done at scale, invasive
  - Single blood lead level does not differentiate between **chronic low-level** and a **single high-level** exposure
  - Lead in blood is from **recent absorption (1 month)** and **long-term bone 'stores' (years)** slowly released into blood during remodelling
  - Adults store 94% blood in bone/teeth; children store 70% in bone/teeth
- Remediation
  - Blood lead levels may take time to drop as lead is mobilised from bone before excretion
  - **Serial blood levels** required to monitor removal

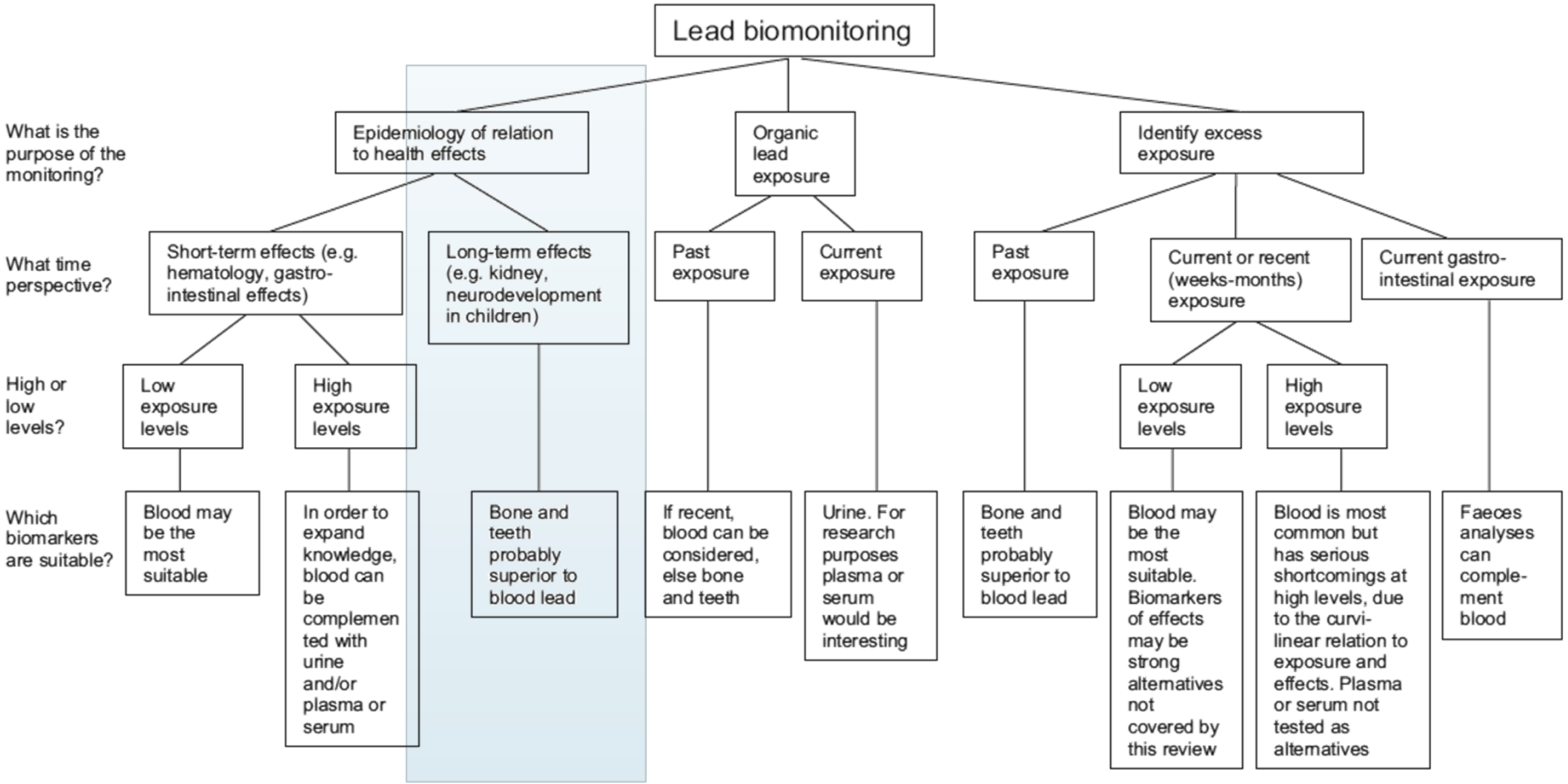


- Research using blood lead levels as a biomarker
  - Associations between **blood lead and long-term outcomes** may be weak due to blood being a poor biomarker of chronic exposure

Measuring exposure – alternative biomarkers

Biomarker	Properties
Plasma/serum	• Invasive; measure of recent absorption and bone release • Low concentration – loss of precision; requires sensitive equipment • Red cell breakdown can contaminate sample
Urine	• Non-invasive; associated with blood/plasma lead • Reliable at low levels of exposure • Requires sensitive analysis equipment • Less quality assurance between labs
Bone	• Higher levels needed to detect (high-level exposure) • Total body burden; linked to blood levels • Specialist imaging techniques – x-ray fluorescence • Higher cost to measure
Teeth	• Shed teeth – non-invasive • High levels – and timing of exposure • Specialised measurement – expensive • Possible variation between teeth in same child; or by sex/age
Hair/nails	• Contamination is a problem (even after washing)
Faeces	• Potentially useful for recent gut ingestion

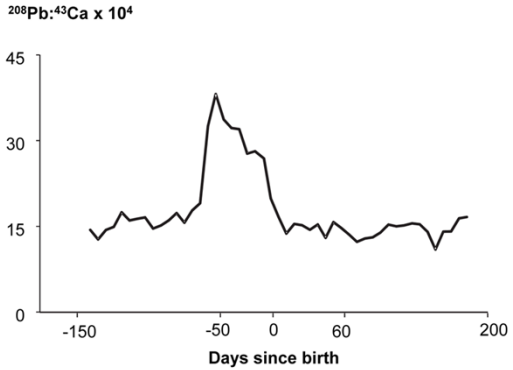
Choice of biomarker

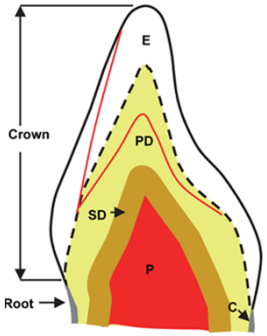


Bergdahl & Skerfving. *J Toxicol Env Health* 2008;71:1235-43

Measuring lead in shed milk teeth

- Hare et al. J Dent 2011;39:396-403 – spatial distribution of lead in teeth
  - Laser-ablation inductively-coupled plasma mass spectrometry (LA-ICP-MS
  - Demonstrated that it was possible to analyse pre- and post-natal accumulation of lead (and other trace elements) in teeth
  - Neonatal line is formed at birth in secondary dentine – samples can be taken across this line corresponding to exposure of fetus and child

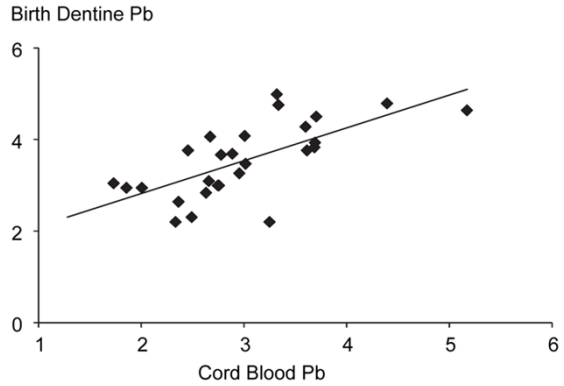




- Shepherd et al. Sci Total Environ. 2012;425:214-22 – lifetime exposure
  - Between tooth variation within child was negligible

Correlation of teeth lead with other measures

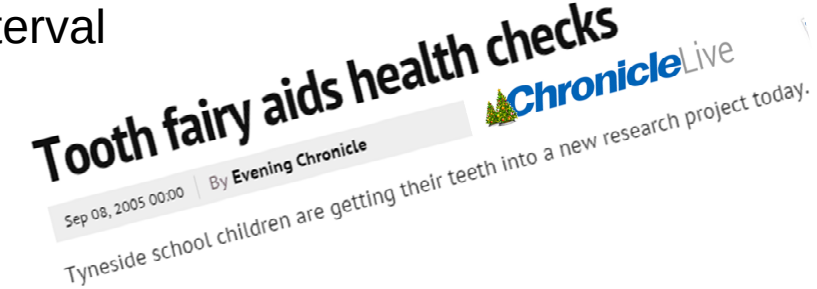
- Arora et al. Plos One 2014 – pregnancy cohort exposure to lead
  - 85 pregnant women in prospective Mexican birth cohort
  - Compared teeth (dentine) lead with pregnancy samples of mother's blood lead, mother's bone lead, umbilical cord blood lead and serial blood lead samples from the child up to 6 years
  - Lead levels in **dentine formed at birth** were significantly associated with **cord blood lead**
  - Lead levels in **prenatally formed dentine** correlated with **maternal patella** (kneecap) lead levels
  - Lead in **dentine formed at 3 months** of age were significantly associated with **child's blood lead** sampled concurrently



- Confirmed tooth lead is a valid measure of exposure over time

Tooth Fairy project – Newcastle

- Regional study of shed milk teeth in Newcastle
  - 69 children donated shed milk teeth (aged 5-8 years) in 2005
  - Children born since legislation to reduce lead in water, paint and petrol
- LA-ICP-MS analysis
  - Sampling from pre- and post-natally formed dentine and enamel
  - Not selected by specific time interval


Tooth fairy aids health checks

ChronicleLive

Sep 08, 2005 00:00 | By Evening Chronicle

Tyneside school children are getting their teeth into a new research project today.

- Results
  - Lead levels were low but varied between children
  - No significant associations with sex, age, residence characteristics and renovations, house-cleaning, diet, socio-economic status

Hodgson et al. J Exp Sci Env Epidemiol 2014

Millennium Cohort Study (MCS)

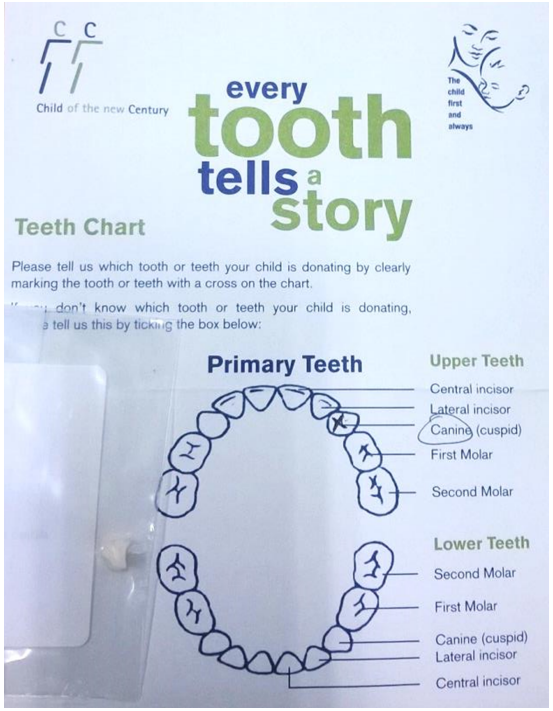
- MCS – Children of the New Century
  - National birth cohort following the lives of around 19,000 children born in the UK in 2000-01
  - Five surveys: at age 9 months; 3, 5, 7 and 11 years

  - Individual data collected includes:
    - Breast/bottle-feeding
    - Cigarette-smoking
    - Parental employment and education
    - Income and poverty measures
    - Housing and neighbourhood – incl. house moves
    - Ethnicity
  - Outcomes at 3, 5 and 7 years of age include
    - Parent assessment of behaviour (standardised questionnaires)
    - Weight and height
    - Reading/vocabulary/maths assessment (7 years)

Child of the new Century

Every Tooth Tells a Story

- MCS collection of shed milk teeth collection (Prof C Dezateux)
  - During the age 7 years survey, children were asked to donate any milk teeth that fell out
  - Posted to us in a small plastic bag (no lead contamination)
  - Over 4100 teeth were received from over 3000 children
  - Most teeth were incisors (>2000)
  - Also 320 canine teeth and 240 molars
  - 300 children donated more than one tooth
- Initial evaluation (ongoing)
  - To evaluate the representativeness of the sample of children who provided teeth in relation to the rest of the cohort



Research Questions

- What is the distribution of lead concentrations in the deciduous teeth of a population sample of children representative of all regions of the UK?

- How do these concentrations vary by:
  - Sex
  - Socio-economic status
  - Ethnic group
  - Ward type and area of residence
  - Early feeding patterns (breast and bottle-feeding)?

- What is the associated on tooth lead concentration with measures of **early childhood motor and intellectual development**?

- How well do current **area-based ecological** measures of lead exposure predict **individual** exposure?

Pilot analysis

- A pilot analysis of 50 teeth will be undertaken within the next 6 months using LA-ICP-MS
  - Analysis overseas to take advantage of laboratory which is able to process teeth at-scale

- Aim of pilot analysis
  - Establish and refine the serial measurements of lead and other trace elements – e.g. strontium, cadmium, manganese – to provide data on lead exposure before birth and up to 7 years of age
  - To explore the association with ecological measures of lead exposure collected in the MCS (CORINE land use; ONS rural/urban designation)

- No feedback about individual measurements will be given to families

Conclusions

- Children are particularly vulnerable to environmental lead exposure:
  - behaviours
  - body processes
- Shed milk teeth have an advantage over blood lead as a biomarker for measuring chronic exposure over time in children
  - including pre-natal and postnatal exposure
- Birth cohort studies allow analysis of individual longer-term outcomes
  - relating to lead exposure at a critical period of development

Acknowledgements

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