IQ and blood lead from 2 to 7 years:

Are the effects in older children the residual of high blood leads in 2 year olds?

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Blood lead concentration

- In US children, blood lead tends to peak at about 2 years, and then decline.
  - Prenatal exposure
  - Postnatal exposure: leaded paint (most houses built before 1980 contain some leaded paint), dust

Dietrich et al. Neurotoxicol Teratol 1993
Meta-analysis of prospective studies

Prospective studies: estimated change in full scale IQ (and 95% CI) for increase in blood lead from 10 to 20 µg/dl

Pocock et al. BMJ 1994

Meta-analysis results:
(a) 0.2 (-1.0, 1.4)
(b) -1.9 (-2.8, -0.9)
(c) -0.9 (-2.0, 0.3)
Implication of peak lead effect

- To study threshold, need to recruit 2 year olds and follow them
- Screening of lead poisoning focusing on 1 and 2 year olds
- Clinical trials treating 2 year olds
Previous prospective studies

- In Boston, 57 mo and 10 y blood lead not associated with 10 y IQ
- In Cincinnati, mean blood lead during the 5th and 6th year associated with IQ at 6.5 years, but mean blood lead during the 2nd or 3rd year was not.
- In Rochester, concurrent blood lead and 5y IQ association slightly stronger than peak blood lead and 5y IQ association
- No study examined the question in detail
Study questions

- What is the strength of the association between blood lead and IQ at various time points?

- Do the cross-sectional associations seen in school age children represent residual effects from peak blood lead?
Treatment of Lead-exposed Children (TLC) study

- Randomized placebo-controlled clinical trial of succimer, an oral chelator
- 1° outcome – IQ
- 780 children aged 12-33 months with blood lead concentration 20-44 μg/dL
- Follow-up to 60 months after treatment (age 7)
- Multi-center: Baltimore, Newark, Philadelphia, and Cincinnati
Lead and IQ measurements

- Blood lead level (PbB)
  - randomization (baseline); day 7, 28, 42 of each course of treatment; every 3-4 months in the follow-up

- IQ
  - Mental Development Index (MDI) from Bayley Scale of Infant Development-II (BSID-II) at baseline
  - Full scale IQ from Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) at 36 month follow-up
  - Full scale IQ from Wechsler Intelligence Scale for Children-III (WISC-III) at 60 month follow-up
  - Caregivers’ IQ (88% mother) from Wechsler Adult Intelligence Scale-Revised (WAIS-R)
Blood lead level in TLC study
No IQ difference from treatment

60 mo follow-up

36 mo follow-up
Statistical analysis

- General linear models
- Untransformed blood lead
- Covariates: Clinical center, race/ethnicity, sex, language, parent’s education, parent’s employment, single parent, age at blood lead test, caregiver’s IQ
- No treatment effect on IQ, so succimer and placebo groups combined
Step 1

PbB baseline  36 mo follow-up  60 mo follow-up
(2y)                  (5y)                    (7y)
2y MDI             5y IQ                 7y IQ
Step 1

PbB baseline   36 mo follow-up   60 mo follow-up
(2y)                  (5y)                    (7y)
2y MDI             5y IQ                 7y IQ
Step 2

- Both prior and concurrent PbB in the model

- $5yIQ = 2yPbB + 5yPbB + \text{Covariates}$

- $7yIQ = 2yPbB + 7yPbB + \text{Covariates}$

- $7yIQ = 5yPbB + 7yPbB + \text{Covariates}$
Results

- 396 children in succimer group, 384 in placebo group (total 780)
- Overall: African American 77%
  - Male 56%
  - Speaking English 95%
  - Parent < high school education 40%
  - Single parent 72%
  - On public assistance 97%
## IQ by PbB modeled separately

<table>
<thead>
<tr>
<th>Outcome</th>
<th>β (95% CI) per 10 μg/dL PbB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2y</td>
</tr>
<tr>
<td>2y MDI</td>
<td>-2.9 (-4.7, -1.0)</td>
</tr>
<tr>
<td>5y IQ</td>
<td>-2.3 (-4.1, -0.5)</td>
</tr>
<tr>
<td>7y IQ</td>
<td>-1.1 (-2.9, 0.7)</td>
</tr>
</tbody>
</table>

All adjusted for center, race, sex, language, parent’s education, employment, single parent, caregiver’s IQ and age at PbB test.
### Both prior and concurrent PbB in the model

<table>
<thead>
<tr>
<th>Outcome</th>
<th>( \beta ) (95% CI) per 10 ( \mu g/dL ) PbB</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2y PbB</td>
</tr>
<tr>
<td>5y IQ</td>
<td>-1.2 (-3.1, 0.7)</td>
</tr>
<tr>
<td>7y IQ</td>
<td>0.1 (-1.8, 2.0)</td>
</tr>
<tr>
<td>7y IQ</td>
<td></td>
</tr>
</tbody>
</table>

All adjusted for center, race, sex, language, parent’s education, employment, single parent, caregiver’s IQ and age at both PbB tests.
### Step 3

- Categorize prior and concurrent PbB into one variable (by corresponding medians)
- To reduce but may not eliminate possible collinearity.

<table>
<thead>
<tr>
<th>Category</th>
<th>2y PbB ($\mu$g/dL)</th>
<th>5y PbB ($\mu$g/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (ref)</td>
<td>&lt;Median$_{2y}$</td>
<td>&lt;Median$_{5y}$</td>
</tr>
<tr>
<td>2</td>
<td>&lt;Median$_{2y}$</td>
<td>$\geq$Median$_{5y}$</td>
</tr>
<tr>
<td>3</td>
<td>$\geq$Median$_{2y}$</td>
<td>&lt;Median$_{5y}$</td>
</tr>
<tr>
<td>4</td>
<td>$\geq$Median$_{2y}$</td>
<td>$\geq$Median$_{5y}$</td>
</tr>
</tbody>
</table>
### 2y and 5y PbB on 5y IQ

<table>
<thead>
<tr>
<th>PbB (μg/dL)</th>
<th>n</th>
<th>5y IQ Mean</th>
<th>5y IQ Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>2y</td>
<td>5y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;24.9</td>
<td>&lt;11.4</td>
<td>227</td>
<td>84</td>
</tr>
<tr>
<td>&lt;24.9</td>
<td>≥11.4</td>
<td>137</td>
<td>79, -2.9 (5.8, 0.1)</td>
</tr>
<tr>
<td>≥24.9</td>
<td>&lt;11.4</td>
<td>138</td>
<td>82, 0.4 (-2.5, 3.3)</td>
</tr>
<tr>
<td>≥24.9</td>
<td>≥11.4</td>
<td>228</td>
<td>78, -4.0 (-6.6, -1.5)</td>
</tr>
</tbody>
</table>

All adjusted for center, race, sex, language, parent’s education, employment, single parent, caregiver’s IQ and age at both PbB tests.
## 2y and 7y PbB on 7y IQ

<table>
<thead>
<tr>
<th>PbB (µg/dL)</th>
<th>n</th>
<th>7y IQ Mean</th>
<th>7y IQ Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>2y &lt; 24.9</td>
<td>187</td>
<td>89</td>
<td>referent</td>
</tr>
<tr>
<td>2y ≥ 24.9</td>
<td>121</td>
<td>89</td>
<td>-0.0 (-2.8, 2.7)</td>
</tr>
<tr>
<td>7y &lt; 7.2</td>
<td>195</td>
<td>84</td>
<td>-3.7 (-6.2, -1.3)</td>
</tr>
<tr>
<td>7y ≥ 7.2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All adjusted for center, race, sex, language, parent’s education, employment, single parent, caregiver’s IQ and age at both PbB tests.
## 5y and 7y PbB on 7y IQ

<table>
<thead>
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<th>PbB (μg/dL)</th>
<th>n</th>
<th>7y IQ Mean</th>
<th>7y IQ Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>5y</td>
<td>7y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;11.4</td>
<td>&lt;7.2</td>
<td>244</td>
<td>89</td>
</tr>
<tr>
<td>&lt;11.4</td>
<td>≥7.2</td>
<td>52</td>
<td>86</td>
</tr>
<tr>
<td>≥11.4</td>
<td>&lt;7.2</td>
<td>62</td>
<td>88</td>
</tr>
<tr>
<td>≥11.4</td>
<td>≥7.2</td>
<td>255</td>
<td>84</td>
</tr>
</tbody>
</table>

All adjusted for center, race, sex, language, parent’s education, employment, single parent, caregiver’s IQ and age at both PbB tests.
Strengths and limitations

- Large sample size, degree of testing, quality control, longitudinal, high retention rate

- Restricted population, no Home Observation for Measurement of the Environment (HOME) score
Conclusions

- We found a stronger relationship between PbB at 7y and IQ at 7y than between IQ at 7y and the higher 2y PbB.
- The strength of the cross-sectional association increases over time.
- Results support the idea that lead exposure continue to be toxic to children as they reach school age, not all the damage was done by the time children were 2-3 year old.
Implication

- Lead exposure at about school age may affect cognition, and it is better to always keep PbBPbB low

- The difficulties in preventing lead exposure ↑, but the potential for prevention ↑
Future work

- To examine the strength of the prospective and cross-sectional associations of lead and IQ using other cohorts
  - Individual cohort
  - Pooled or meta-analysis of several cohorts
Future work

- To study the prevention strategy that keeps blood lead low till school age and IQ improvement
  - Specific population in US with high lead exposure
  - Children in developing countries
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- Harvard University
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