

# ANBI 159: Biological and cultural perspectives on intelligence

## Lecture 25: Epigenesis of IQ

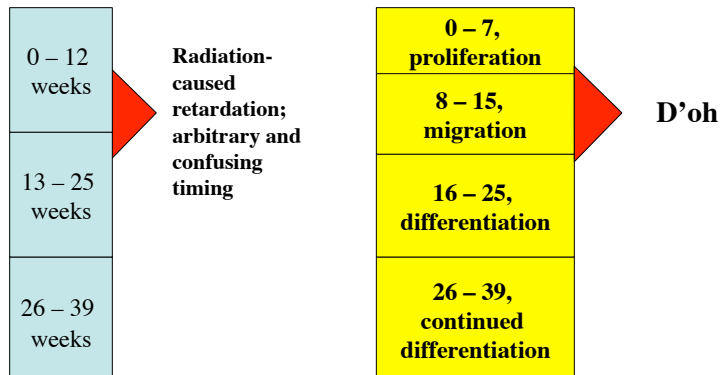
<http://weber.ucsd.edu/~jmoore/courses/>



**Radiation** Note especially the significance of precise timing during pregnancy  
*The Mind* 4m 52s

## Cultural v. biological divisions of pregnancy

Trimesters (9 evenly divisible by 3)



## Lead

- Example of policy success
- Policy changes reduced exposures from paint & gasoline
- Good public awareness



Slide by Dr. Bonnie Nagel, UCSD Psychiatry

U.S. Environmental Protection Agency For more information on preventing lead poisoning call 1-800-424-LEAD or visit www.epa.gov/lead. LEAD Paint Program

**Lead** is poisonous; binds to proteins, can cleave tRNA, alters opioid receptors, inhibits protein filtration by kidneys... variety of mechanisms.

[Formerly?] present in paints, gasoline (tetraethyl lead, anti-knock, in 1920s), solder (tin cans, pipes), as well as various natural sources.

Evidence suggests is concentrated by hippocampus.

## Lead in Federal Register

HUD (1996, Federal Register): “meta-analysis estimated 0.257 IQ points lost per one  $\mu\text{g}/\text{dl}$  increase in blood levels”.

Infers linear relationship between lead & IQ loss, AND

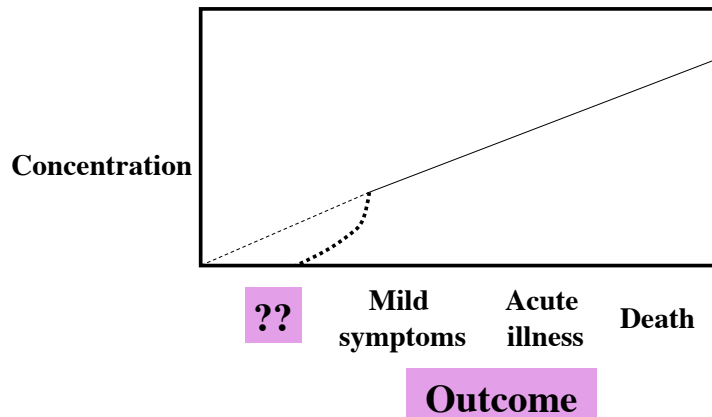
It’s meaningful to talk about tenths of an IQ point.

$\mu\text{g}/\text{dl}$  = microgram/deciliter (1/1,000,000 of a gram per 1/10th liter)

## Lead - linear relationship?

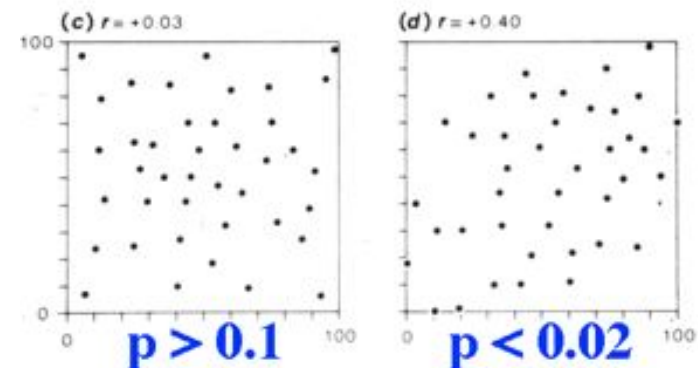
Dose - response curves and scientific certainty

Infers linear relationship between lead & IQ loss,



## Lead - tenths of an IQ point?

It’s meaningful to talk about tenths of an IQ point.



## The Yugoslavia Prospective lead study

Study: Late 70s reports of correlations between lead & school performance; several long-term prospective studies initiated.

1985: Recruit pregnant women at clinics in Kosovo, Yugoslavia to participate in longterm research. Range of lead exposures greatest in any project to date.

Kosovska Mitrovica (lead smelter, refinery, battery plant; heavily contaminated)

Pristina (University town, 25 miles away; low levels)

Start with  $\approx 1,300$  pregnancies; exclude obvious birth defects etc., not all parents agree, eventually  $\approx 600$  followed pregnancy to 7.5 years, and  $\approx 300$  with full samples blood, intelligence tests, home descriptions, etc.

Blood sampled every 6 months. Wasserman et al. 1997, Factor-Litvak et al. 1999

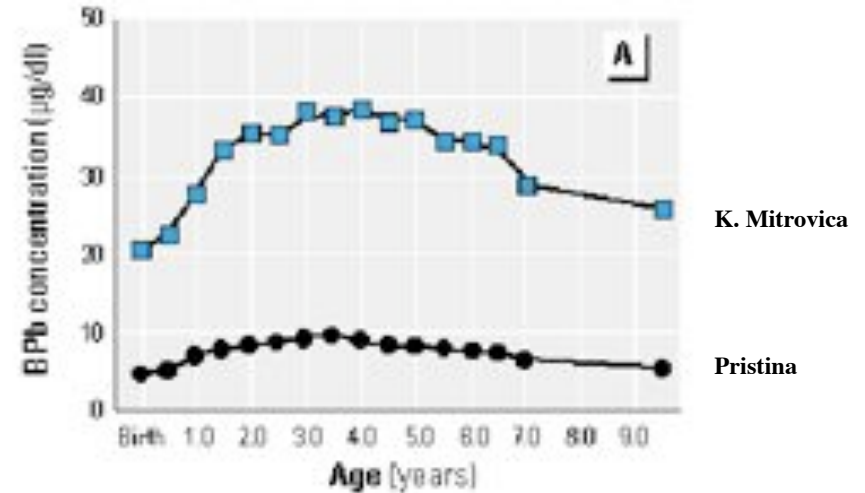


Figure 1. Mean concentrations of blood lead (BPb) for Kosovska Mitrovica and Pristina by age

Factor-Litvak et al. 1999

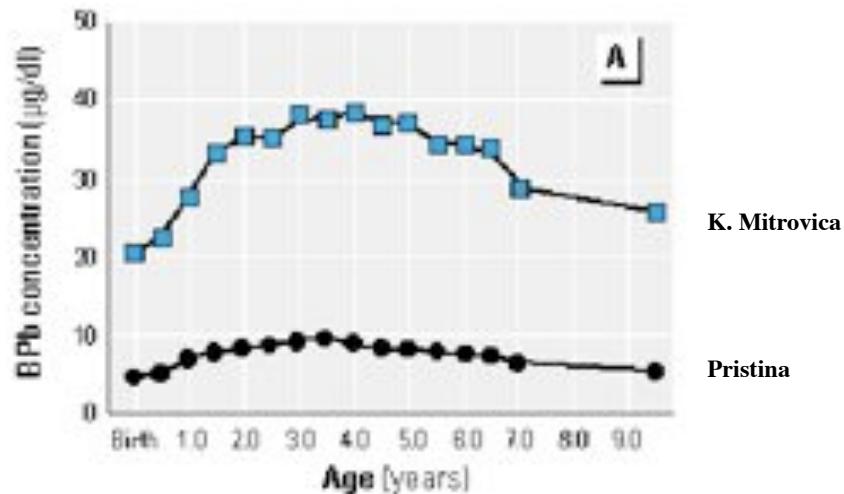


Figure 1. Mean concentrations of blood lead (BPb) for Kosovska Mitrovica and Pristina by age

Why the decrease??

Factor-Litvak et al. 1999

## Lead x IQ: results negligible[?]

Simple correlations between total cumulative lead exposure and intelligence measures not significant; slopes negative but negligible -- e.g., - 0.05

Adjusting for covariates, another story. Multiple regression results presented as residuals.

# Confounds/covariates

Regression models included several covariates that were chosen, in part, to facilitate comparisons with other published studies.

Covariates included

- gender,
- sibship size at the time of the IQ test,
- birth weight
- ethnicity: Serbian, Albanian, other
- HOME score *Home Observation for Measurement of the Environment*
- years of maternal education
- maternal age
- maternal Raven's test score

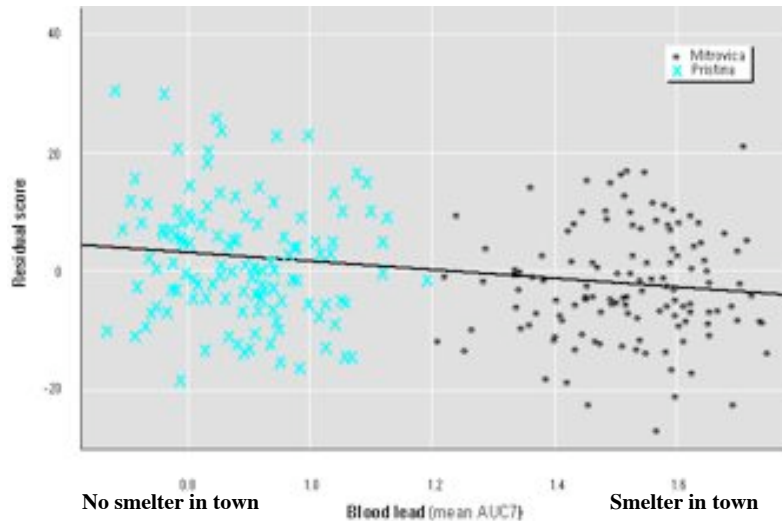
**Table 1.** Relationships between blood lead (BPb) concentration at age 4, General Cognitive Index (GCI) of the McCarthy Scales of Children's Abilities, and measures of the social environment in Kosovska Mitrovica and Pristina, Yugoslavia

Variable	Kosovska Mitrovica		Pristina	
	GCI	BPb	GCI	BPb
HOME Score				
4-21	65.7 ±12.0	38.7 ±11.7	74.5 ±12.9	10.1 ±3.9
22-26	80.4 ±13.5	40.2 ±10.3	79.6 ±10.3	10.3 ±3.1
27-31	80.1 ±17.2	37.7 ±11.9	90.2 ±11.3	9.4 ±2.6
32-35	82.1 ±14.8	40.9 ±11.3	91.3 ±12.8	9.7 ±3.3
36-49	96.4 ±15.5	40.6 ±8.3	99.9 ±16.2	8.2 ±2.8
<u>Maternal Education (years)</u>				
None	68.7 ±15.3	38.5 ±12.2	68.0 ±11.5	11.4 ±5.7
1-8	75.3 ±14.9	38.2 ±11.2	79.8 ±13.0	9.6 ±2.9
9-12	87.6 ±16.6	41.9 ±11.1	93.7 ±15.1	9.4 ±3.0
≥13	98.3 ±11.3	43.0 ±8.2	97.1 ±23.7	8.6 ±4.6
<u>Maternal Raven Score<sup>a</sup></u>				
4-17	69.8 ±13.7	37.1 ±11.2	77.1 ±14.5	9.2 ±2.4
18-26	78.9 ±19.4	41.0 ±10.8	81.4 ±15.5	10.9 ±4.7
27-35	78.9 ±11.3	37.4 ±12.2	88.3 ±15.7	8.8 ±2.7
36-43	83.8 ±16.4	40.2 ±8.6	90.4 ±12.7	9.9 ±2.5
44-60	91.4 ±17.7	44.2 ±11.2	98.5 ±17.7	9.3 ±3.4

HOME, Home Observation for the Measurement of the Environment. Values shown are mean ± standard deviation.  
<sup>a</sup>Raven's Progressive Matrices.

GCI ≈ IQ

Factor-Litvak et al. 1999



**Figure 2 .** Covariate-adjusted Full Scale IQ (residual scores) across levels of cumulative lead exposure. AUC7, area under the blood lead \* time curve at age 7 years. **AUC7 - cumulative lead exposure to age 7**  
 Wasserman et al 1997

**Table 2.** Associations between blood lead (BPb) concentration and measures of cognitive development in Kosovska Mitrovica and Pristina, Yugoslavia

Cognitive measure	Age (years)	$\beta^a$	$\beta^b$	CI <sup>c</sup>
Bayley Scales of Infant Development	2			
Mental Development Index		-3.3	-5.3	(-10.1--0.5)
McCarthy Scales of Children's Abilities	4			
Global Cognitive Index		-7.1	-9.4	(-14.2--4.6)
Perceptual Performance		-6.6	-7.1	(-10.2--3.9)
Verbal		-0.8	-2.7	(-5.4--0.1)
Quantitative		-5.5	-5.9	(-9.6--2.0)
Memory		-1.0	-3.2	(-5.6--0.5)
Motor		-2.6	-4.3	(-6.3--0.0)
Wechsler Intelligence Scales for Children-III	7			
Full Scale IQ		-4.7	-9.0	(-12.4--5.5)
Performance IQ		-4.5	-9.4	(-13.3--5.6)
Verbal IQ		-3.7	-7.1	(-10.5--3.7)

CI, 95% confidence interval; Hgb, hemoglobin.

<sup>a</sup>Unadjusted regression coefficient for log<sub>10</sub> BPb concentration, adjusted only for Hgb measured concurrently with the cognitive measure.

<sup>b</sup>Adjusted regression coefficient for log<sub>10</sub> BPb concentration, is adjusted concurrently with the cognitive measure. All adjusted regression coefficients adjusted for home observation for measurement of the environment score, ethnic group (Serbian, Albanian, other), maternal age, birth weight (kg), maternal Raven's Progressive Matrices score, maternal education (years), birth order (ages 2 and 4) or sibship size (age 7), and sex. All ages 2 and 4, we also adjusted for Hgb concentration at the time of cognitive testing.

<sup>c</sup>CI for selected CI, adjusted for the full set of covariates.

Factor-Litvak et al. 1999

**Table 2.** Associations between blood lead (BPb) concentration and measures of cognitive development in Kosovska Mitrovica and Pristina, Yugoslavia

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<sup>c</sup>CI for unadjusted, adjusted for the full set of covariates.

Spatial/quantitative selectively affected

Factor-Litvak et al. 1999

## Lead x IQ and SES

We expected no associations between Pb and SES in our Yugoslavia sites. However, prior to data collection, **new housing within 2 km and downwind of the smelter was built in K. Mitrovica. Occupants had higher education, IQ, and HOME scores.** Thus, our unadjusted estimates of association between Pb and cognition were biased downward.

**IE, Better-off people moved to new housing, which had higher lead exposure, result was masking effects of lead.**

## Lead and height

Just a little something to think about...

Average heights at age 7 same in both towns, but in Pristina only, find negative relationship between lead and height at age 4.

**“In Pristina, where BPbs ranged from approximately 1 µg/dl to 14 µg/dl, height decreased by 7.3 cm (CI, 1.8-12.8) per log unit increase in BPb.”**

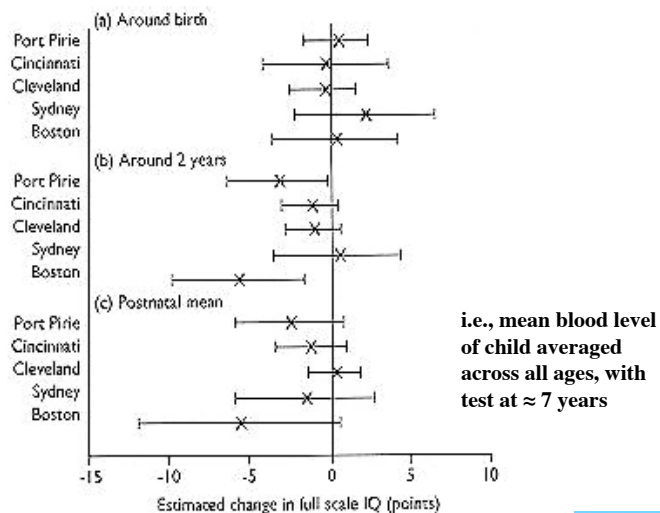
**IE, only had effect at low concentrations.** Recall, < 10 µg/dl = “safe” by CDC. *If real*, (1) dose-response not linear, and (2) developmental effect within US “safe” range.

OK, that’s Yugoslavia...

**There have been MANY studies of the lead - intelligence/behavior relationship, and precise details still controversial.**

**Look at one meta-analysis.**

FIG 1 - **Prospective studies:** estimated change in full scale IQ (and 95% confidence interval) for increase in blood lead from 10 to 20 {micro}g/dl, using three measures of blood lead in each study



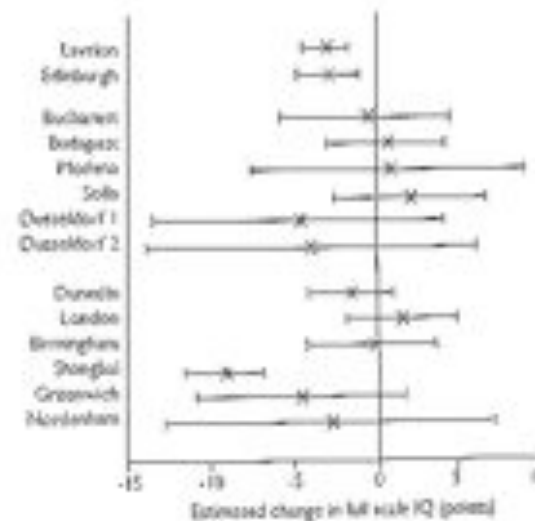
NB: published prior to 1994, so Yugoslavia study not included.

Pocock, S J et al. BMJ 1994;309:1189-1197 REVIEW

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FIG 2 - **Cross sectional blood lead studies:** estimated change in full scale IQ (and 95% confidence interval) for increase in blood lead from 10 to 20 {micro}g/dl

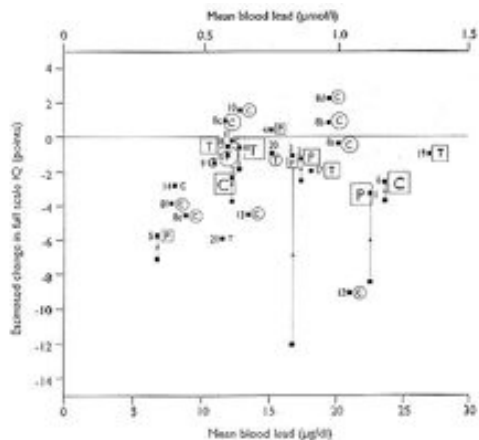


Pocock, S J et al. BMJ 1994;309:1189-1197 REVIEW

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FIG 4 - **Overall synthesis of 26 studies** relating lead concentrations to IQ. For each study the estimated change in IQ for a specific doubling of body lead burden (10 to 20 {micro}g/dl blood lead or 5 to 10 {micro}g/g tooth Lead) is plotted against the study's mean blood lead concentration. Study types: P=prospective, C=cross sectional blood lead, T=cross sectional tooth lead. Three sizes of letter represent the size of the study (>400, 200-400, or <200 children). Substantial or partial adjustment for confounders is indicated by a square or circle respectively; the influence of substantial adjustment is shown by the arrowed lines. The number of each point identifies the study's reference (see tables)



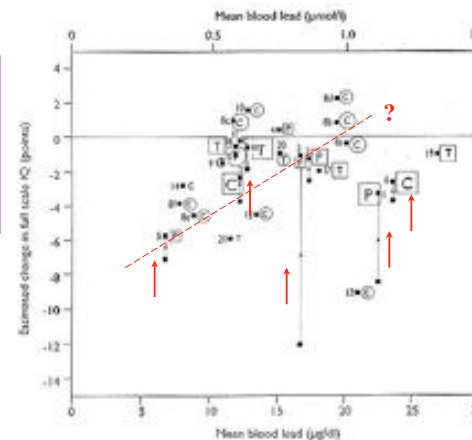
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There is no striking relation between the studies' mean blood lead and the magnitude of the lead-IQ association...



Pocock, S J et al. BMJ 1994;309:1189-1197 REVIEW

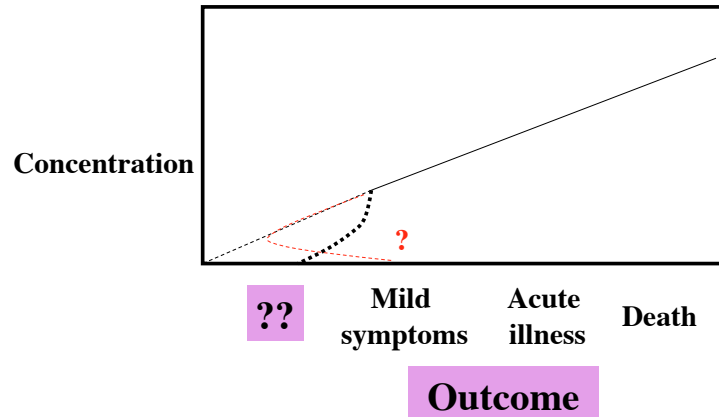
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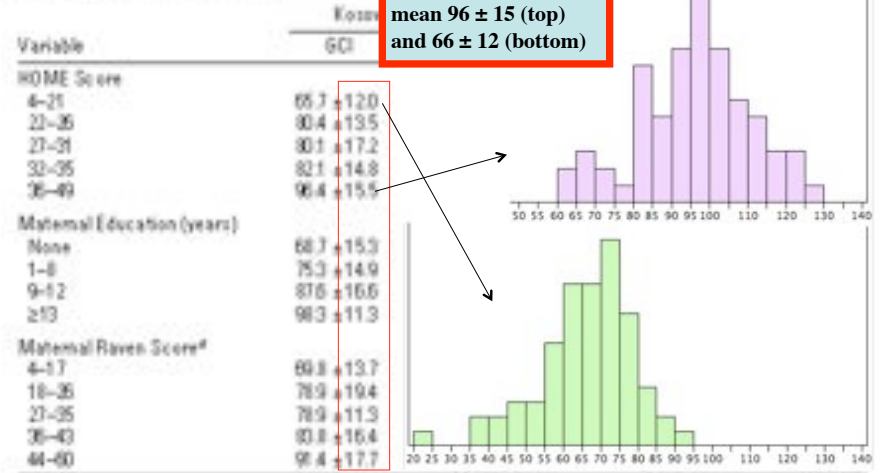
# Lead

Dose - response curves and scientific certainty

**Infers linear relationship between lead & IQ loss,**



**Table 3.** Relationships between blood lead (BPb) concentration at age 4, General Cognitive Index (GCI) of the McCarthy Scales of Children's Abilities, and maternal education in Kosovo's Mitrovica and Pristina, Yugoslavia



Variance in GCI  $\approx$  IQ

How *strong* is the effect of lead, relatively?

## Lead in perspective

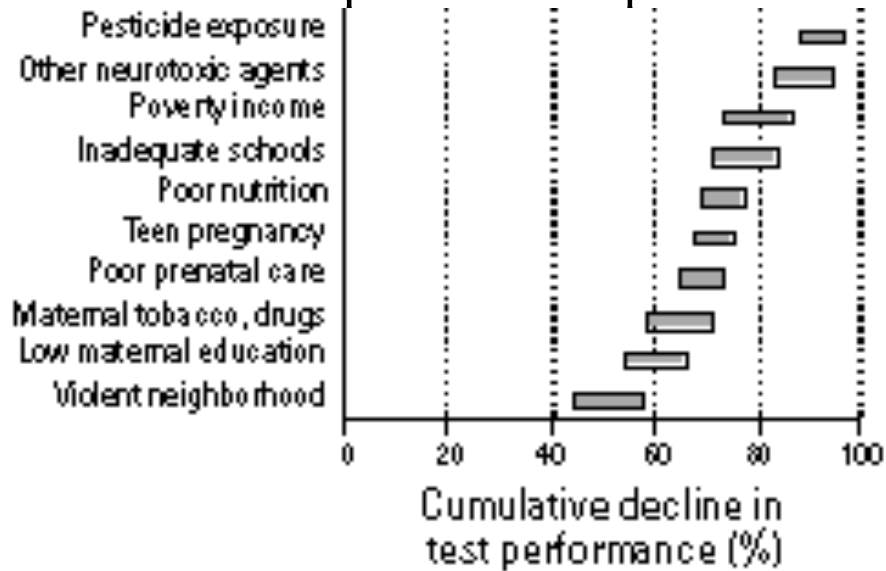
Lead exposure explained 2 - 4% of variance in IQ at age 7

## Lead in perspective

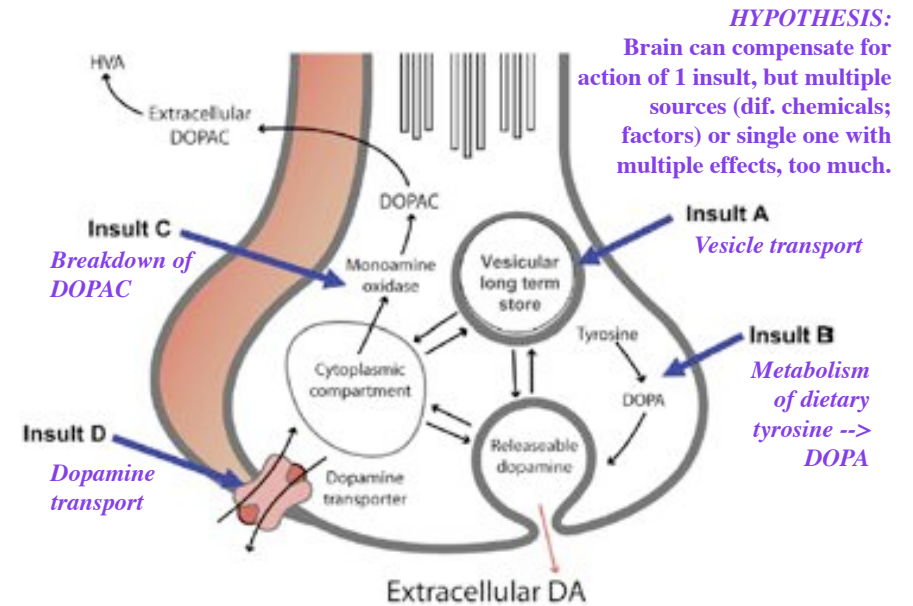
Lead exposure explained 2 - 4% of variance in IQ at age 7

Home environment (HOME score) at age 3-4 explained 25 - 30%

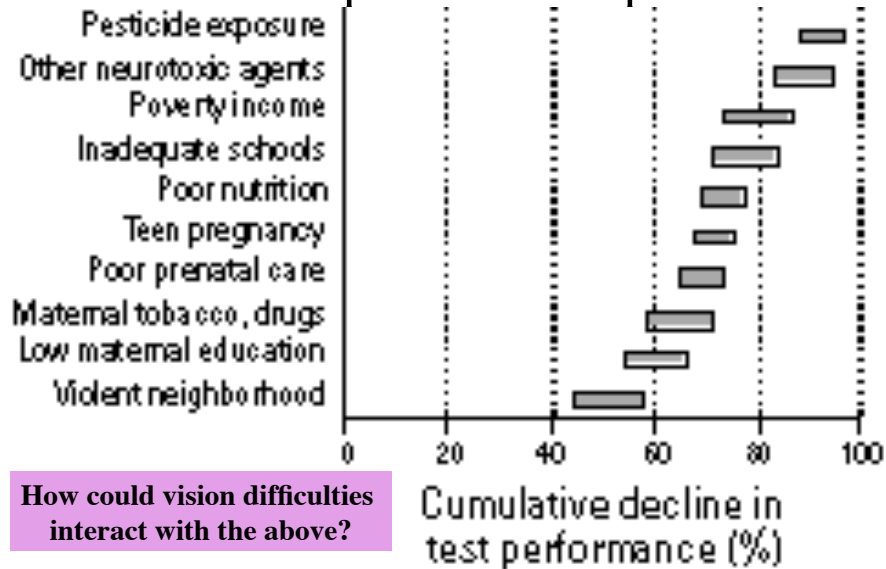
## Cumulative impacts - conceptual model



## Dopamine systems: multiple impacts



## Cumulative impacts - conceptual model



How could vision difficulties interact with the above?

## Back to lead: Yes, but is it a *problem*?

“Low blood levels” of lead:  $\approx 10 - 20 \mu\text{g/dl}$

Below 10 is considered “safe” and over 20, treatment advised (CDC). 2004 USA average:  $\sim 1-2 \mu\text{g/dl}$

$10 * 0.257 \text{ IQ points per } \mu\text{g/dl} = 2.57 \text{ IQ points.}$

So what?

### Cost of IQ loss

**10 \* 0.257 IQ points per  
 $\mu\text{g}/\text{dl} = 2.57$  IQ points.**

**So what?**

Studies find lower IQ associated with

- 1) lower salary for those who work, and
- 2) lower probability of working (via poorer school performance)

**In 1999 \$, between \$13,000 - 17,000 lower income over lifetime for *each* IQ point.**

### Cost of IQ loss

**10 \* 0.257 IQ points per  
 $\mu\text{g}/\text{dl} = 2.57$  IQ points.**

**So what?**

**\$30,000 - 40,000 over each individual's lifetime translates into billions of dollars over the population as a whole.**

### Cost of IQ loss

**10 \* 0.257 IQ points per  
 $\mu\text{g}/\text{dl} = 2.57$  IQ points.**

**So what?**

**\$30,000 - 40,000 over each individual's lifetime translates into billions of dollars over the population as a whole.**

**One estimate (slightly different basis):**

**> \$100 billion / year**

**Ounce of prevention worth  
\$100,000,000,000 of cure...**

*... and that analysis fails to account for senile dementia at the end of life ...*

## Model of Pb - related cognitive decline

L.D. White et al. / Toxicology and Applied Pharmacology 225 (2007) 1–27

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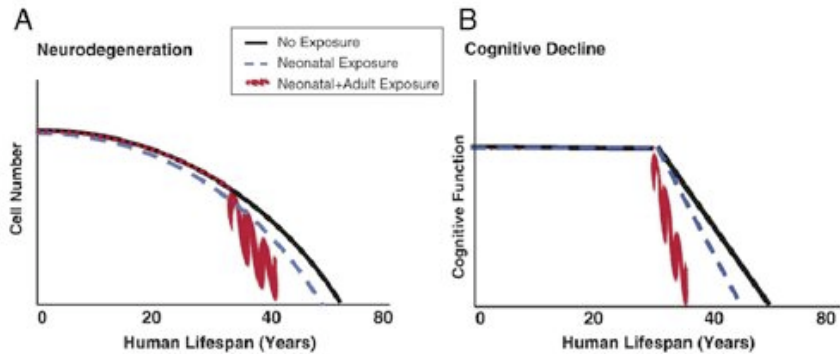


Fig. 9. Hypothetical model showing the relationship between chemical exposure, neurodegeneration, and cognitive decline. Cells are lost in a gradual manner early in adulthood; however, cognitive decline is not evident until the aging period. In panel A, a model of cellular loss in the brain is displayed.

Evidence growing that Alzheimer's Disease is promoted by Pb exposure when young.

## Cumulative impacts - conceptual model

