



Putting it into Practice: Pediatric Environmental Health Training Resource

Childhood Lead Poisoning



Children's
Environmental
Health
Network



Author

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Outline: Key Points

- I. Introduction: How much lead is too much for a child?
- II. Sources/Pathways of Exposure
- III. Epidemiology of Clinical Effects
- IV. Overt Signs and Symptoms of Lead Poisoning
- V. Diagnosis and Treatment



I. Introduction: How much lead is too much for a child?

- Until 2012, the CDC “level of concern” was 10 $\mu\text{g}/\text{dL}$
- Term “level of concern” **no longer used** by CDC because *all* levels are of concern and *no* level can be considered “safe”
- “Level of concern” replaced by “reference value”



I. Introduction: How much lead is too much for a child? (continued)

- Reference level *is not* health-based, but defined as the 97.5th percentile of distribution of blood lead levels in U.S. children 1-5 years old, based on NHANES survey
- Current reference level is $5 \mu\text{g/dL}$
- Will be re-considered every 4 years on basis of the two most recent NHANES surveys (next in 2016)



II. Sources/Pathways of Exposure

Lead is a Multi-media pollutant

Major sources/pathways

- Lead-based paint (homes built pre-1978)
 - Approximately 24 million housing units contain deteriorated lead-based paint



Lead Paint & Lead Hazards U.S. Housing, 1999

<u>Year built</u>	<u>% w/ Pb paint</u>	<u>% w/ Pb hazards</u>
before 1940	87%	68%
1940-1959	69%	43%
1960-1977	24%	8%
1978-1998	3%	1%





II. Sources/Pathways of Exposure (continued)

- Other sources/pathways
 - Dust (integrates lead from deteriorated paint, soil lead tracked inside, deposition of airborne lead)
 - Water (usually corrosion of older fixtures or lead solder connecting pipes)
 - Food (imported foods such as ground spices, food prepared or stored in lead-glazed pottery)

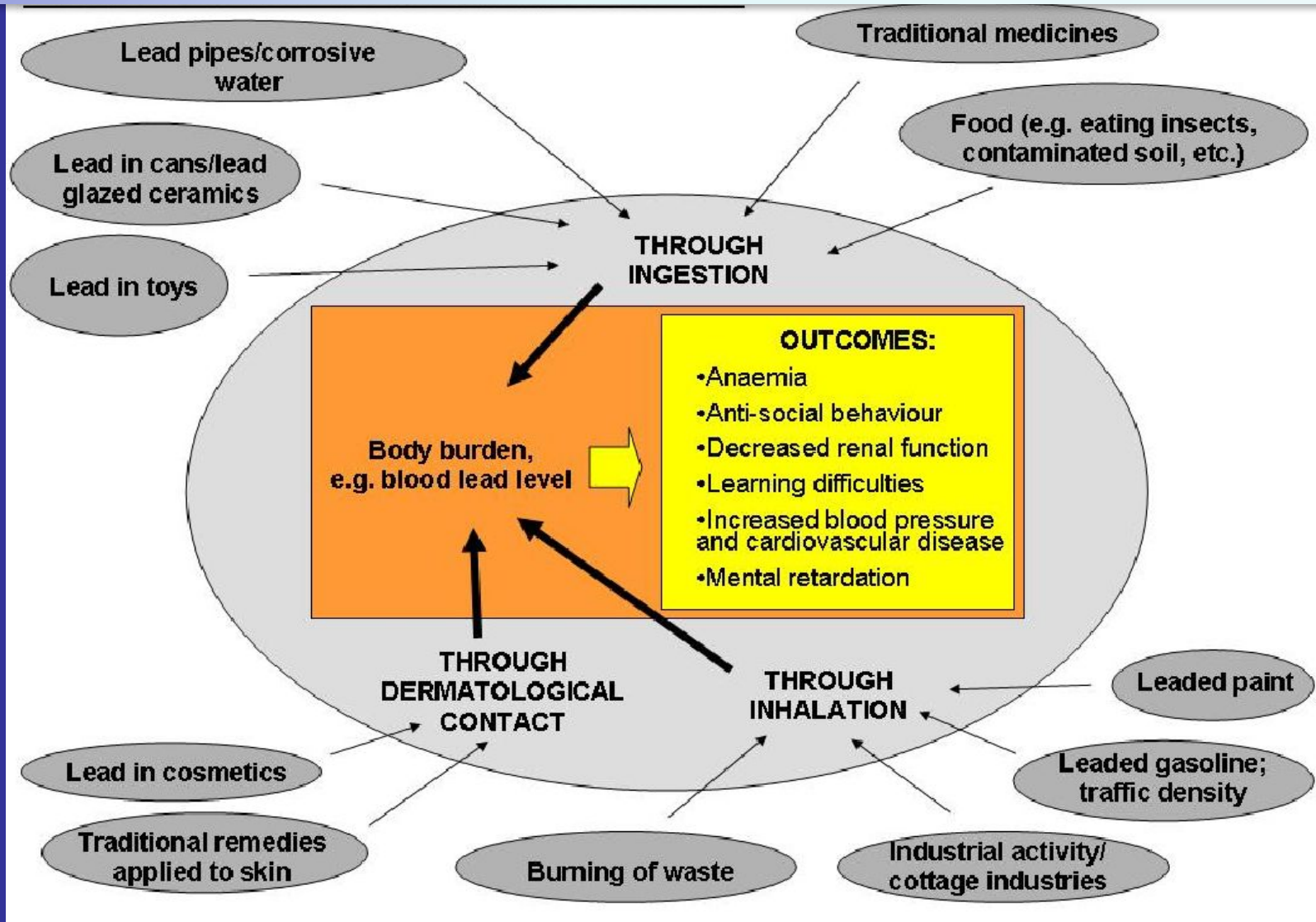


II. Sources/Pathways of Exposure (continued)

- Alternative or complementary medicines, herbs, or therapies (e.g., Ayurvedic medicines)
- Cosmetics (kohl, surma)
- Lead-painted toys (older or imported)
- Adult activities (e.g., “take home” from occupation, hobbies involving use of lead)

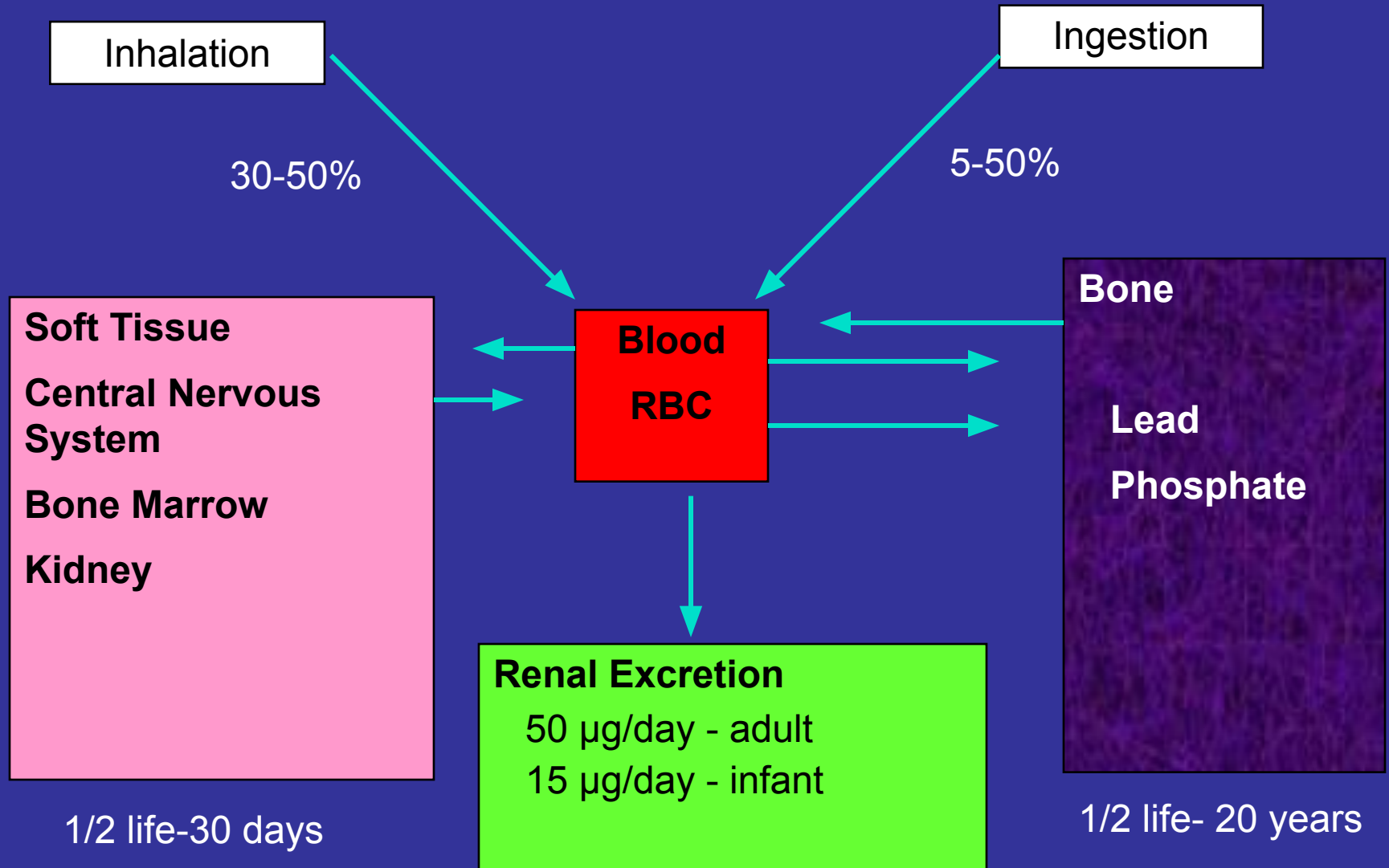


Sources of Child's Exposures to Lead



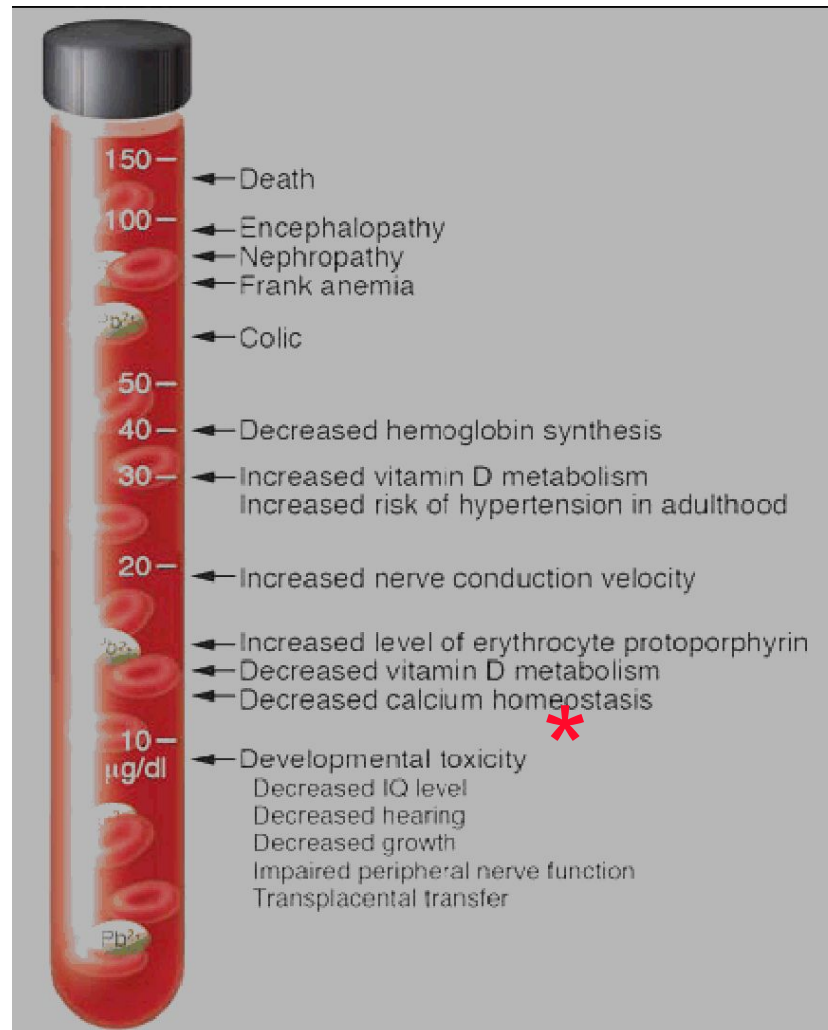


III. Epidemiology of Clinical Effects Related to Exposure: Metabolism of Lead





Blood Lead Levels at Which Adverse Effects Observed in Different Organ Systems in Children



***Developmental toxicity has been observed at levels of 1-2 µg/dL; 10 µg/dL is *NOT* a threshold**



Effects of Early Lead Exposure on the Developing Brain

- Apoptosis
- Excitotoxicity
- Decreased cellular energy metabolism
- Impaired heme synthesis
- Oxidative stress
- Lipid peroxidation
- Altered activity of second messenger systems
- Altered neurotransmitter release and receptor densities



Effects of Early Lead Exposure on the Developing Brain

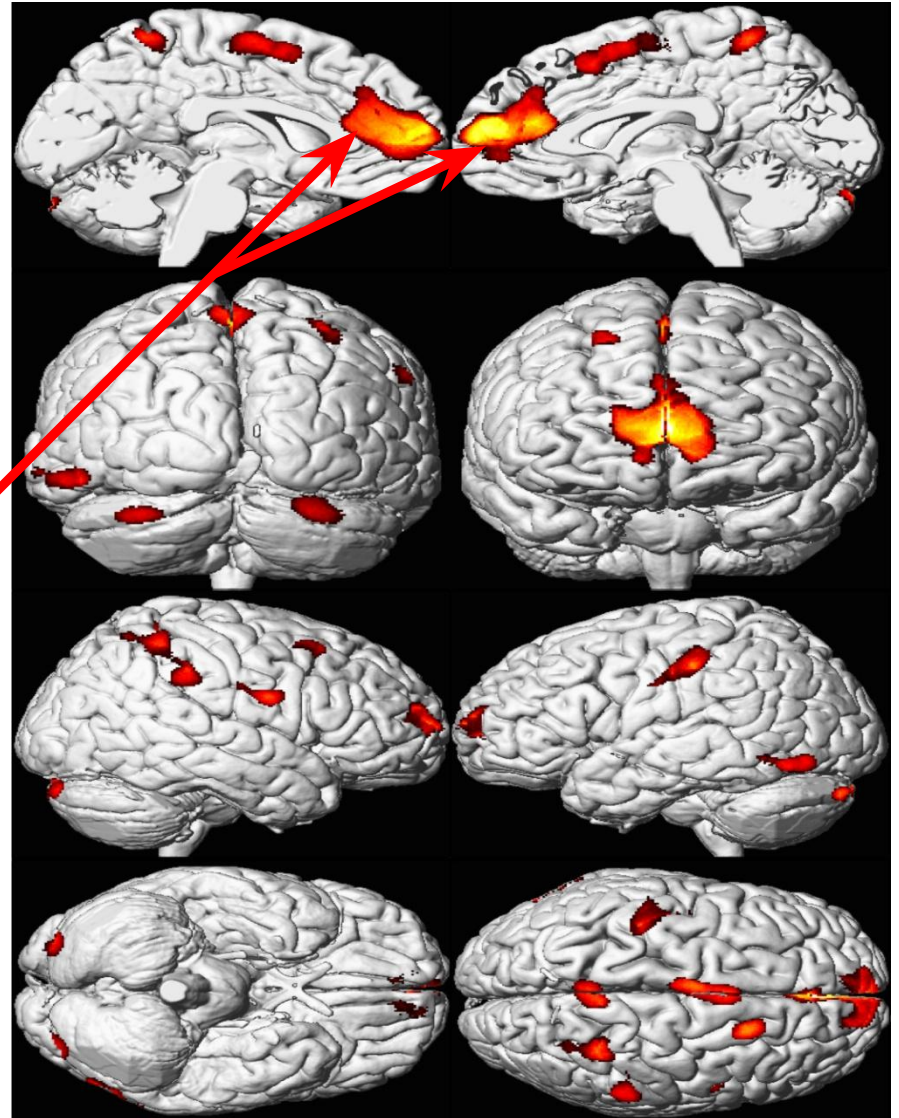
- Impaired development and function of oligodendroglia
- Abnormal myelin formation
- Abnormal neurotrophic factor expression
- Abnormal dendritic branching patterns
- Disruption of blood-brain barrier
- Disruption of thyroid transport into brain
- Altered regulation of gene transcription



Brain Volume

Volumetric MRI Studies Reveal Decreased Brain Volumes in Adults (19-24 years old) with Greater Childhood Lead Exposure

- Red/yellow areas indicate brain regions with significant *volume loss* associated with greater blood lead level in childhood
- Loss greatest in *frontal* area of brain





Childhood Lead Exposure and Organization of White Matter in Young Adults

- Diffusion tensor imaging (DTI) is a neuroimaging modality useful in detecting abnormalities in white matter fiber structure in the brain
- DTI in young adults lead-exposed as children reveals persistent dose-related changes in white matter microstructure suggesting *altered myelination and axonal integrity*



Childhood Lead Exposure and Brain Metabolism in Young Adults

- Magnetic resonance spectroscopy (MRS) is a neuroimaging modality useful in detecting changes in metabolic activity in the brain
- MRS studies in young adults lead-exposed as children reveal dose-related changes in:
 - Gray matter, consistent with irreversible neuronal dysfunction
 - White matter, consistent with permanent alterations to myelin structure



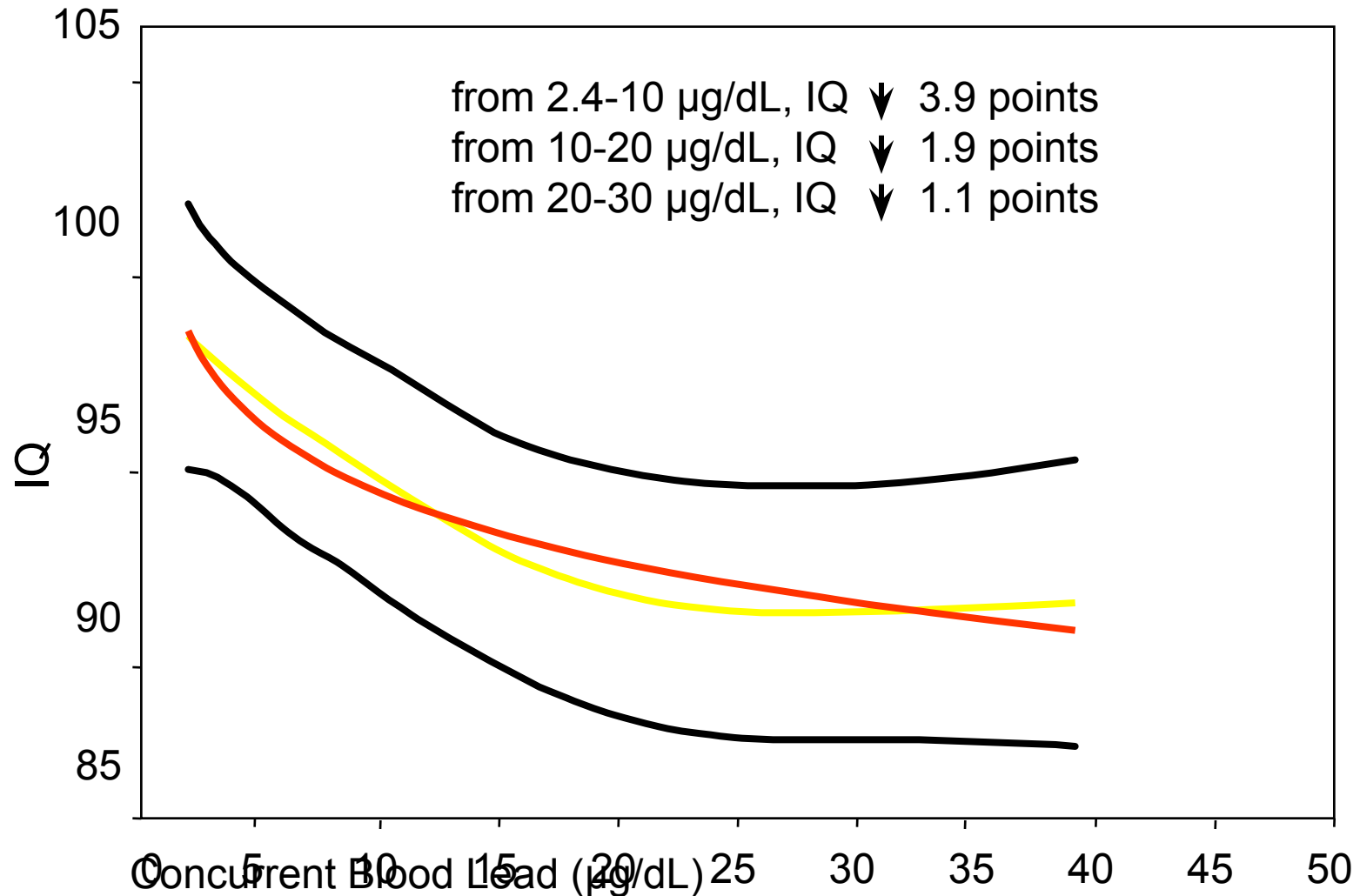
Neuropsychological Deficits Associated with Lead Poisoning

No “signature injury” but studies have linked a wide array of neurodevelopmental problems to “subclinical” lead levels, including:

- Reduced IQ
- Difficulty maintaining attention
- Impulsivity and hyperactivity
- Visual-perceptual skills
- Executive functions
- Fine motor skills
- Reduced academic achievement

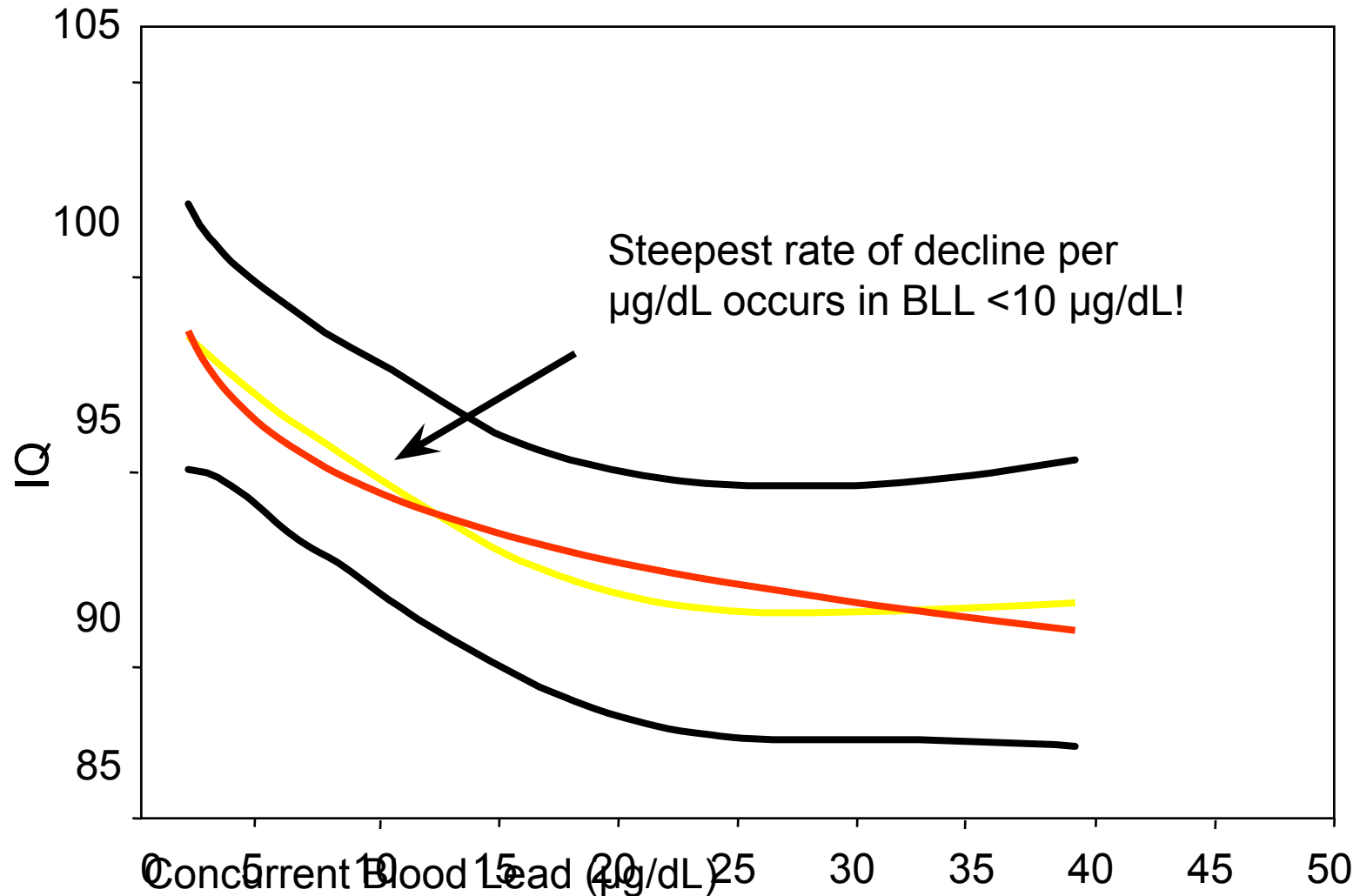


Relationship of Concurrent Blood Lead Level and IQ in a Pooled Analysis of 1,333 Children





Relationship of Concurrent Blood Lead Level and IQ in a Pooled Analysis of 1,333 Children





Blood Lead Level and Academic Achievement Deficits, *Adjusting for Full-Scale IQ*

	5-10 µg/dL*	P-value
<i>Reading Composite</i>	-5.0*	0.02
-Basic Reading	-4.4	0.03
-Reading Comprehension	-4.6	0.02
<i>Math Composite</i>	-3.7	0.03
-Math Reasoning	-2.0	0.18
-Numerical Operations	-4.2	0.03

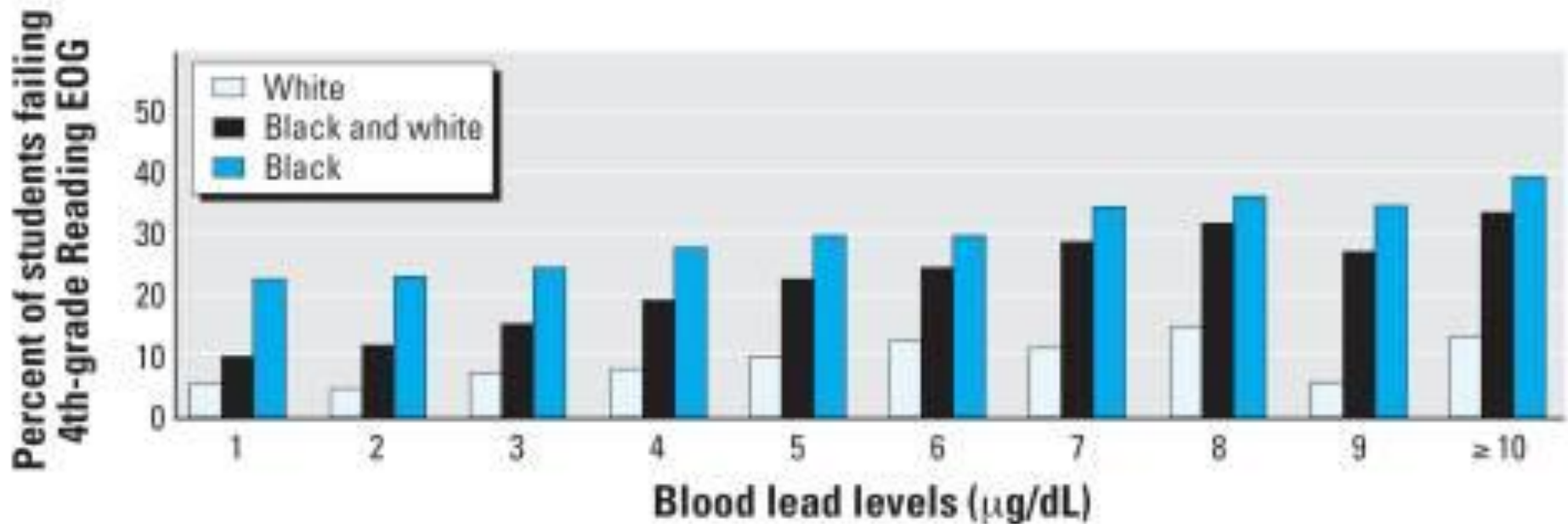
* Referent group: children with BLL of 1-2 µg/dL

Surkan et al. *Neurotoxicology*, 2007.



Blood Lead Levels and Performance on End-of-Grade Reading Achievement Test

2000-2004, NC 4th graders (N=8,600)





Blood Lead Level and ADHD

Adjusted Odds Ratio

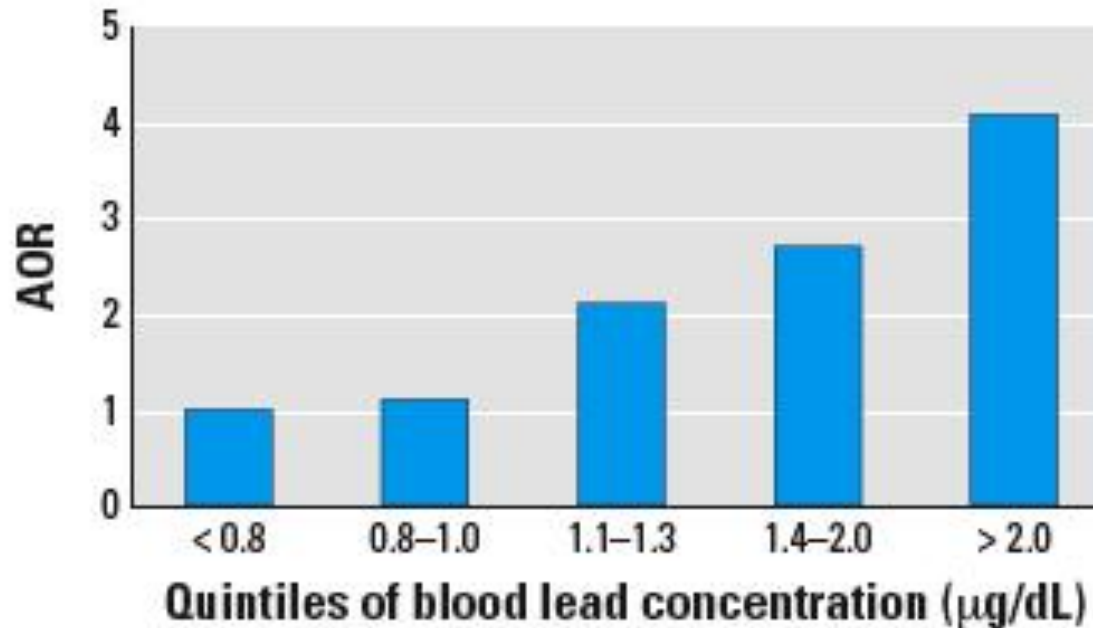


Figure 1. AOR for ADHD among U.S. children, NHANES 1999–2002, by blood lead concentration (µg/dL). The model was adjusted for child's age, sex, race/ethnicity, preschool attendance, serum ferritin, prenatal ETS exposure, smoker in the household, and insurance status.

p-value for trend = 0.012.

Braun et al. *Environ Health Perspect*, 2006.



Early Life Lead Exposure History and Criminal Arrests in Early Adulthood

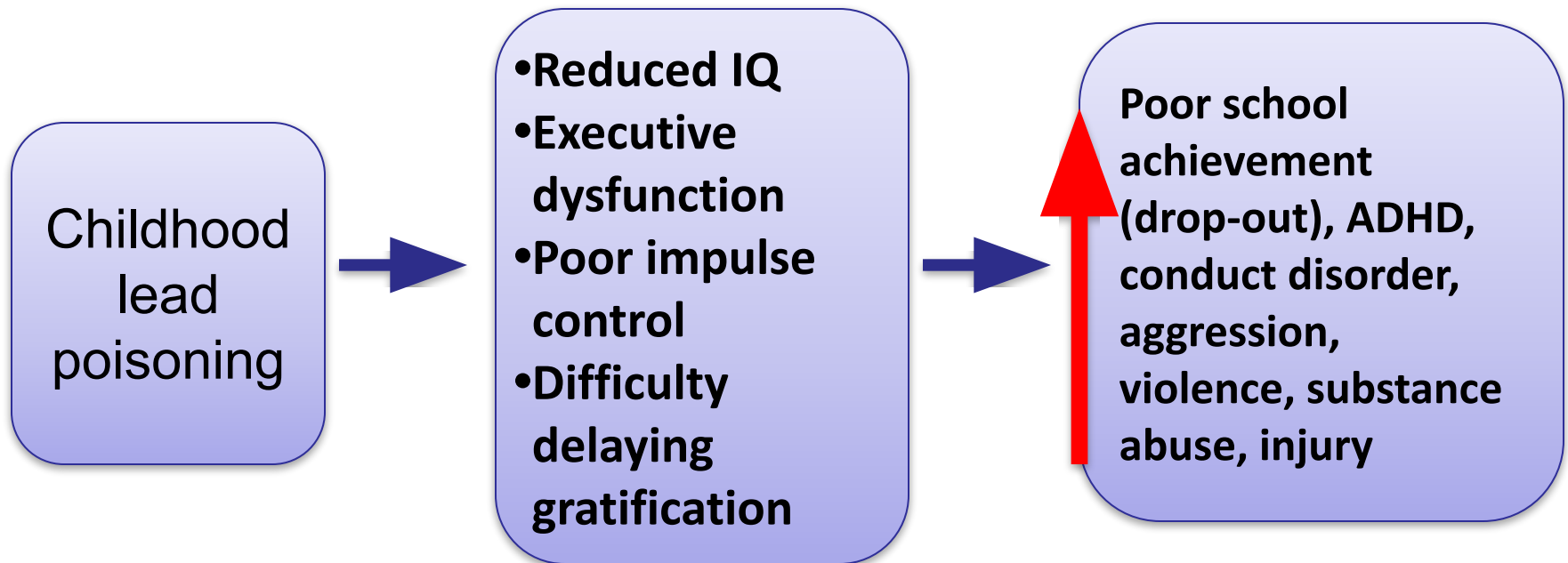
Among 250 19-24 years old followed since birth, likelihood of being arrested (based on county criminal justice records) was significantly associated with:

- Prenatal blood lead level
- Blood lead level at 6 years of age
- Average blood lead level up to 6 years of age



Potential Adverse Outcomes

Hypothesized Chain of Events Linking Early Lead Exposure to Adverse Outcomes in Later Childhood and Adulthood





Lead and Neurodegeneration?

- Studies in animal models (mice, rats, monkeys) suggest that early life lead exposure increases risk of cognitive decline in adulthood
- Increase in beta-amyloid and plaque formation, particularly in *frontal* regions of brain



Are Cognitive Effects of Lead Reversible if Blood Lead Level is Decreased?

- Port Pirie Cohort Study (Australia) analyzed blood lead change vs. cognitive change in childhood, up to age 11-13 years
 - Results: *no significant association* between blood lead reduction and improved cognitive scores
- Treatment of Lead-Exposed Children(TLC) study
 - The *only* randomized clinical trial of chelation of children
 - Chelation of children with baseline blood lead levels of 20-44 $\mu\text{g/dL}$ *did not* improve children's cognitive outcomes



But There is Some Hope for Secondary Prevention!

- Adverse effects of early life lead exposure on learning can be reduced by providing animals with an “enriched” environment (i.e., exposure to other animals, a larger cage, more materials to interact with)
- Poorest learners were animals both exposed to lead and raised in an “impoverished” environment
- Environmental enrichment also resulted in less severe lead-associated disruption of important neurochemical factors in the brain (NMDA receptor, brain-derived neurotrophic factor)



Screening Guidelines, CDC

- Universal screening required at ages 12 and 24 months for Medicaid-enrolled children regardless of lead risk
- CDC (1997) recommended:
 - Blood lead screening be conducted based on local risk factors (due to regional variability in prevalence of risks and elevated levels)



Screening Guidelines, CDC (continued)

- Each state (or city) should formulate own screening recommendations based on local data
- Universal screening for communities with prevalence of >27% of pre-1950 homes or prevalence of blood lead levels (≥ 10 $\mu\text{g/dL}$) in children 12-36 months of $\geq 12\%$
- Targeted screening for specific groups with higher prevalence of risk factors or lower prevalence of elevated blood lead levels



AAP Recommendations to Pediatricians

- Provide anticipatory guidance to parents of all infants and toddlers about preventing lead poisoning.
- Inquire about lead hazards in housing and child care settings.
- Know state Medicaid regulations and measure blood lead level in Medicaid-eligible children.
- Find out if there is relevant guidance from the city or state health department about screening children not eligible for Medicaid. If there is none, consider screening all children.



AAP Recommendations to Pediatricians (continued)

- Be aware of any special risk groups that are prevalent locally, such as immigrants, foreign-born adoptees, refugees, or children whose parents work with lead or lead dust in their occupation or hobby and those who live in, visit, or work on old houses.
- In areas with old housing and lead hazards, encourage application for HUD or other funds available for remediation
- Keep current with the work of the CDC Advisory Committee on Childhood Lead Poisoning Prevention and any relevant local committees.



Screening Guidelines: Pregnant and Lactating Women

- CDC (2010):
 - Pregnant and lactating women should be screened for possible lead exposure based on questionnaire
 - Blood lead level should be measured in women at high-risk for exposure
 - Schedule for follow-up testing provided, as well as for neonates and infants of women with a blood lead level $\geq 5 \mu\text{g/dL}$



IV. Overt Signs and Symptoms of Lead Poisoning

- Lot of inter-individual variability in signs and symptoms
- Few children show any signs or symptoms that are clearly linked to lead until blood lead level reaches 50 $\mu\text{g}/\text{dL}$ or higher
- Signs and symptoms in children with low blood lead levels:
 - Usually NONE
 - Longer-term:
 - Developmental delay
 - Learning problems
 - Reduced attention



IV. Overt Signs and Symptoms of Lead Poisoning (continued)

- Signs and symptoms in children with moderate blood lead levels:
 - constipation
 - poor appetite
 - abdominal pain
 - anemia (usually $>40 \mu\text{g/dL}$)
- Signs and symptoms in children with high blood lead levels:
 - poor appetite
 - vomiting
 - irritability
 - lethargy
 - seizures



Other Etiologies to Consider in Differential Diagnosis

- Bacterial meningitis
- Viral encephalitis
- Obstructive hydrocephalus
- Pseudotumor cerebri
- Ischemic or hemorrhagic stroke (especially in children with sickle cell disease)
- Brain tumors
- Recurrent seizures or status epilepticus
- Non-accidental trauma or other closed head injuries



Lead poisoning should be considered in the differential diagnosis of children who present with variety of neurodevelopmental disorders

- Developmental delay
- Disorders of attention
- Learning disability
- Visual-motor incoordination
- Auditory perceptual deficits
- Language disorders
- Speech problems
- Intellectual disability
- Autistic and other behavioral problems



Physical Examination

- A physical exam of children with a blood lead level $>20 \mu\text{g/dL}$ is recommended to determine:
 1. Whether child has any signs suggesting encephalopathy
 2. Whether child is engaging in high-risk behaviors (e.g., pica, hand-to-mouth activity)
 3. If child has a behavioral or neurodevelopmental disorder requiring referral (e.g., ADHD, oppositional defiant disorder, developmental delay, speech delay)
- Children identified by means of routine blood lead screening might have *no* remarkable findings on physical exam



V. Diagnosis and Treatment

Diagnostic Testing

- In asymptomatic children, most clinical laboratory results (other than blood lead) will be normal
- Iron status (serum iron, total iron binding capacity, serum ferritin)
- Routine assessment of renal function is not indicated (unless child is administered chelating agents)
- Abdominal films might indicate whether child is currently ingesting lead-containing objects (lead lines in long bones generally not present <50 $\mu\text{g/dL}$)



Methods Not Recommended for Use in Diagnosing Lead Poisoning

- Gingival lead lines
- Testing of neurophysiologic function
- Evaluation of renal function (except during chelation with EDTA)
- Testing of lead in hair, teeth, packed red cells, saliva, or fingernails
- Radiographic imaging of long bones
- Provocative chelation (lead mobilization test)



Recommended Schedule for Obtaining a Confirmatory Venous Sample

Blood lead level ($\mu\text{g}/\text{dL}$)	Time to confirmatory testing
Reference level-9	1-3 months
10-45	1 week-1 month*
45-59	48 hours
60-69	24 hours
≥ 70	Urgently as emergency test

*The higher the blood lead level on the screening test, the more urgent the need for confirmatory testing



Schedule for Follow-Up Blood Lead Testing^a

Venous blood lead level (µg/dL)	Early follow-up testing (2-4 tests after identification)	Later follow-up testing after blood lead level declining
Reference value-9	3 months*	6-9 months
10-19	1-3 months*	3-6 months
20-24	1-3 months*	1-3 months
25-44	2 weeks-1 month	1 month
≥45	As soon as possible	As soon as possible

^aSeasonal variation of blood lead levels exists and might be more apparent in colder climate areas; greater exposure in the summer months might necessitate more frequent testing

*Case managers or PCPs might choose to repeat blood lead levels on all new patients within a month to ensure that their level is not rising



Potential Causes of a Blood Lead Rise During Follow-Up

- Unrecognized sources of exposure
- Inappropriate abatement activities
- Failure to mitigate the identified hazard
- Redistribution of lead stores within a child's body
- Laboratory imprecision



Components of Treatment

Four components, depending on a child's blood lead level:

1. Environmental control

- Interrupt pathway(s) of exposure
- Requires a thorough **environmental history***
(example of World Health Organization's Environmental History to follow)

*See also the "Environmental History-Taking" module in CEHN's Pediatric Training Resource



Components of Treatment (continued)

2. Behavior modification (parent)

- Instruction in methods for cleaning up dust and loose paint from surfaces
- Instruct parents to wash child's hands frequently, especially before eating

3. Nutritional counseling

- Address dietary deficiencies in iron and calcium (dietary modification or supplements)

4. Chelation therapy



Environmental History (WHO, 2010)

Characteristics of Child's Residence:

- What is the age and general condition of the residence?
- What was the previous use of the land before the building was constructed?
- Is there evidence of chewed or peeling paint on woodwork, furniture, or toys?
- How long has the family lived in that residence?
- Have there been recent renovations or repairs to the house or building?



Environmental History (WHO, 2010)

Characteristics of Child's Residence (continued):

- Are the windows new?
- What is the condition or composition of indoor play areas?
- Do outdoor play areas contain bare soil that may be contaminated?
- How does the family attempt to control dust and dirt?
- Are painted materials or waste materials burned in household fireplaces or used as combustibles?



Environmental History (WHO, 2010)

Sources of Exposure in Neighborhood

- Does smoke or dust come from external sources close to the building?
- Are there point sources near the home, such as smelters, metallurgic industries, battery recycling activity (even inactive) or open burning of waste?
- Are there other sites at which the child spends significant amounts of time?
- Are there any local idiosyncratic sources or uses of lead?



Environmental History (WHO, 2010)

Child's Behavior

- To what degree does the child exhibit hand-to-mouth activity?
- Does the child exhibit pica?
- Are the child's hands washed before meals and snacks?



Environmental History (WHO, 2010)

Family Factors and Practices

- What are the hobbies of household members? Do they include fishing and preparing weights, working with ceramics or stained glass, hunting and preparing shots for guns, or handicraft activities that use tin or lead solders?
- Does the child receive or have access to imported food, food of unsecure origin, cosmetics or folk remedies?
- Is food prepared or stored in glazed pottery or metal vessels?
- Does the family use foods stored in soldered cans?



Recommended Actions According to Blood Lead Level: Below the Reference Value of 5 $\mu\text{g}/\text{dL}$

- Lead education
 - Dietary
 - Environmental
- Environmental assessment for pre-1978 housing
- Follow-up blood lead monitoring



Recommended Actions According to Blood Lead Level: ≥ 5 but <45 $\mu\text{g/dL}$

- Lead education
 - Dietary (focusing on sufficient calcium, iron, and vitamin C intake)
 - Environmental
- Follow-up blood lead monitoring
- Complete history and physical exam



Recommended Actions According to Blood Lead Level: ≥ 5 but <45 $\mu\text{g/dL}$ (continued)

- Lab work
 - Iron status (consider iron level, total iron binding capacity, serum ferritin)
- Environmental investigation & lead hazard reduction
- Neurodevelopmental monitoring
- Abdominal X-ray if particulate lead ingestion is suspected, with bowel decontamination if indicated



Recommended Actions According to Blood Lead Level: 45-69 $\mu\text{g}/\text{dL}$

- Lead education
 - Dietary (focusing on sufficiency of calcium and vitamin C)
 - Environmental
- Follow-up blood lead monitoring
- Complete history and physical exam
 - Lab work
 - Iron status (consider iron level, total iron binding capacity, serum ferritin)



Recommended Actions According to Blood Lead Level: 45-69 $\mu\text{g}/\text{dL}$ (continued)

- Environmental investigation & lead hazard reduction
- Neurodevelopmental monitoring
- Abdominal X-ray if particulate lead ingestion is suspected, with bowel decontamination if indicated
- Oral chelation therapy, consider hospitalization if a lead-safe environment cannot be assured



Recommended Actions According to Blood Lead Level: $>70 \mu\text{g/dL}$

- Hospitalize and start chelation therapy (following confirmatory venous blood lead test) in conjunction with consultation from a medical toxicologist or a Pediatric Environmental Health Specialty Unit (PEHSU)
- Proceed according to actions for 45-69 $\mu\text{g/dL}$



Chelation

- No recommended changes to the existing CDC guidelines (2002) for evaluation and treatment of children requiring chelation (blood lead level ≥ 45 $\mu\text{g/dL}$)
- If clinician not familiar with treatment protocols, consultation with a medical toxicologist and/or regional PEHSU or a clinician experienced in treating children with chelation therapy is highly recommended
- As mentioned, chelation *does not* reverse adverse effects of lead on children's cognitive development



Case Study 1

- 5-year-old boy with hyperactivity and abdominal colic
- History: mother worked in an automobile repair shop, where the child played
- Exam: height and weight 10th percentile, short attention span, restlessness, delayed speech development, poor social skills



Case Study 1

Laboratory

- Laboratory
 - Microcytic anemia
 - BLL – 30 $\mu\text{g/dL}$
 - Hgb – 10.7 gr/dL; MCV – 72 fL
 - Serum Ca – normal
- Flat abdominal X-ray: no radio-opacities
- BLL in mother – 40 $\mu\text{g/dL}$, referred for follow-up



Case Study 1

Management & Follow up

- Management
 - Abate source: cleaning, avoid further contact with dirty clothes, wash hands
 - Treat anemia with iron supplement
 - No chelation
- Repeat BLL
 - in 1 month – 26 $\mu\text{g/dL}$,
 - in 2 months – 24 $\mu\text{g/dL}$
 - in 3 months – 22 $\mu\text{g/dL}$

Four months later – asymptomatic



Case Study 2

- 7-year-old girl with anemia
- History: lives in Baltimore, Maryland with parents, who say that she peels paint off the wall and digs putty out of the window frames and eats them
- Exam: height and weight 20th percentile, otherwise appears normal



Case Study 2

Laboratory

- Laboratory:
 - Microcytic anemia
 - Hgb – 10.4 g/dL; MCV – 70 fL
 - BLL – 47 $\mu\text{g/dL}$



Case Study 2

Management & Follow up

- Management
 - Remove from home while remediation occurs
 - Treat anemia with iron supplement
 - No chelation
- Repeat BLL
 - in 1 month – 38 $\mu\text{g/dL}$,
 - in 2 months – 35 $\mu\text{g/dL}$
 - in 3 months – 30 $\mu\text{g/dL}$



Summary of Key Points

How much lead is too much for a child?

- Until 2012, the CDC “level of concern” was 10 $\mu\text{g}/\text{dL}$
- Term “level of concern” **no longer used** by CDC because *all* levels are of concern and *no* lead level can be considered “safe”
- “Level of concern” replaced by “reference value”



Key Points (continued)

How much lead is too much for a child? (continued)

- Reference level *is not* health-based, but defined as the 97.5th percentile of distribution of blood lead levels in U.S. children 1-5 years old, based on NHANES survey
- Current reference level is $5 \mu\text{g/dL}$
- Will be re-considered every 4 years on basis of the two most recent NHANES surveys (next in 2016)



Key Points (continued)

Sources/Pathways of exposure

- Lead-based paint most common source of high blood lead levels
- Lead in house dust an important pathway for children with lower blood lead levels



Key Points (continued)

Sources/Pathways of exposure (continued)

- The myriad of sources/pathways of exposure requires a thorough **environmental history**^{*} for a child with a blood lead level above the reference value, focusing on the child's residence, behaviors, and family factors and practices

^{*}See also the "Environmental History-Taking" module in CEHN's Pediatric Training Resource



Key Points (continued)

Epidemiology of Clinical Effects

- Children can effectively absorb up to 50% of the lead they ingest
- Lead moves from blood to soft tissues
- Some is excreted, but most travels to bone where it has a $\frac{1}{2}$ life of 20 years and can be leached back into the blood



Key Points (continued)

Epidemiology of Clinical Effects (continued)

- Central nervous system is the organ system *most* vulnerable in lead poisoning
 - Higher childhood lead exposure associated altered:
 - Brain growth
 - Brain organization
 - Brain function



Key Points (continued)

Epidemiology of Clinical Effects (continued)

- Higher blood lead levels associated with:
 - IQ loss
 - Reduced academic achievement
 - Neuropsychological deficits
 - Behavioral disorders (e.g., ADHD)
- Neurodevelopmental deficits associated with early life exposure are persistent, likely irreversible, as they are still present in young adults



Key Points (continued)

Diagnosis and Treatment

- The primary basis for diagnosing lead poisoning is blood lead level, as children might be otherwise asymptomatic
- Recommended management, including schedule for obtaining a confirmatory venous blood sample, for follow-up blood lead testing, and interventions depend on a child's blood lead level



Key Points (continued)

Diagnosis and Treatment

- Treatment has four components
 - Environmental control
 - Behavior modification (parents)
 - Nutrition counseling
 - Chelation therapy
- Chelation therapy *does not* reverse lead's adverse effects on children
- Primary prevention of exposure is critical in reducing the morbidities associated with childhood lead exposure



Key References

- CDC. Managing Elevated Blood Lead Levels Among Young Children: Recommendations from the Advisory Committee on Childhood Lead Prevention (2002).
(http://www.cdc.gov/nceh/lead/CaseManagement/caseManage_main.htm)
- AAP. Lead exposure in children: prevention, detection, and management. (2005). *Pediatrics*, 116:1036-46.
- CDC. Guidelines for the Identification and Management of Lead Exposure in Pregnant and Lactating Women (2010).
(<http://www.cdc.gov/nceh/lead/publications/LeadandPregnancy2010.pdf>)
- CDC. Low Level Lead Exposure Harms Children: A Renewed Call for Primary Prevention (2012).
(http://www.cdc.gov/nceh/lead/ACCLPP/Final_Document_030712.pdf)
- World Health Organization. Childhood Lead Poisoning (2010).
(<http://www.who.int/ceh/publications/childhoodpoisoning/en/>)



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