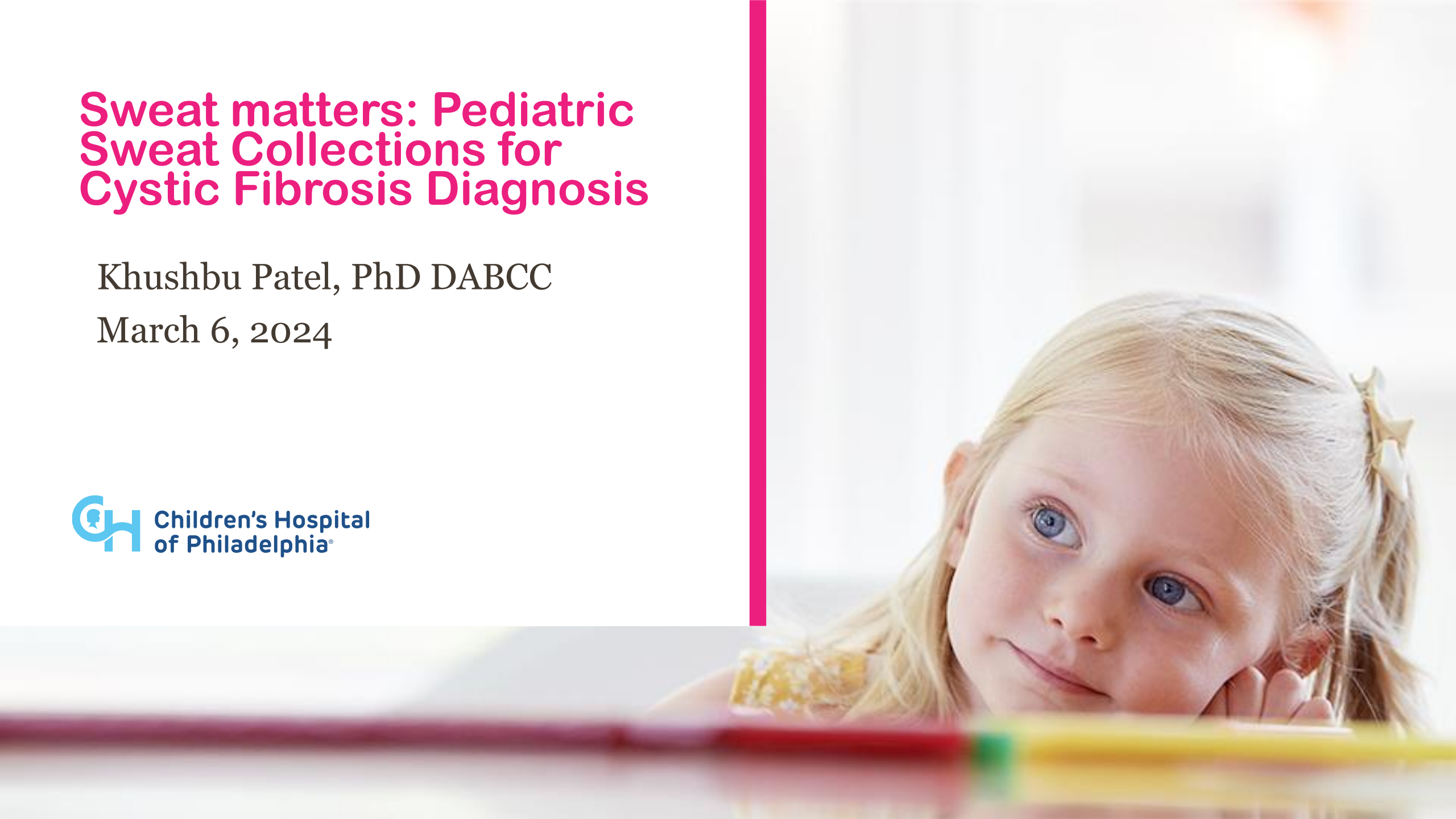
Sweat matters: Pediatric Sweat Collections for Cystic Fibrosis Diagnosis

Khushbu Patel, PhD DABCC

March 6, 2024

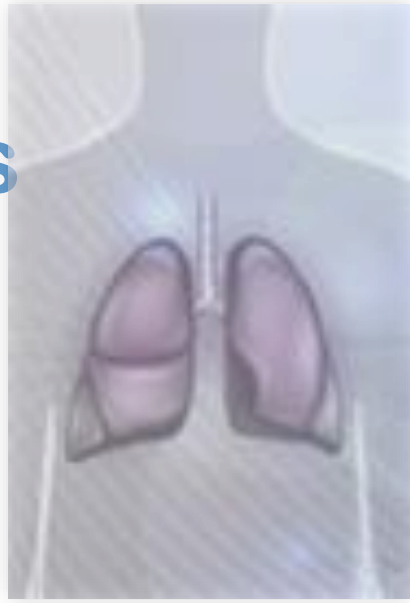
Children's Hospital of Philadelphia®



Learning Objectives

- Discuss how sweat chloride analysis is used for diagnosis of cystic fibrosis
- Understand how sweat collection and testing methodologies work
- List factors that influence optimal sweat collection

Cystic Fibrosis and Diagnostic Approaches

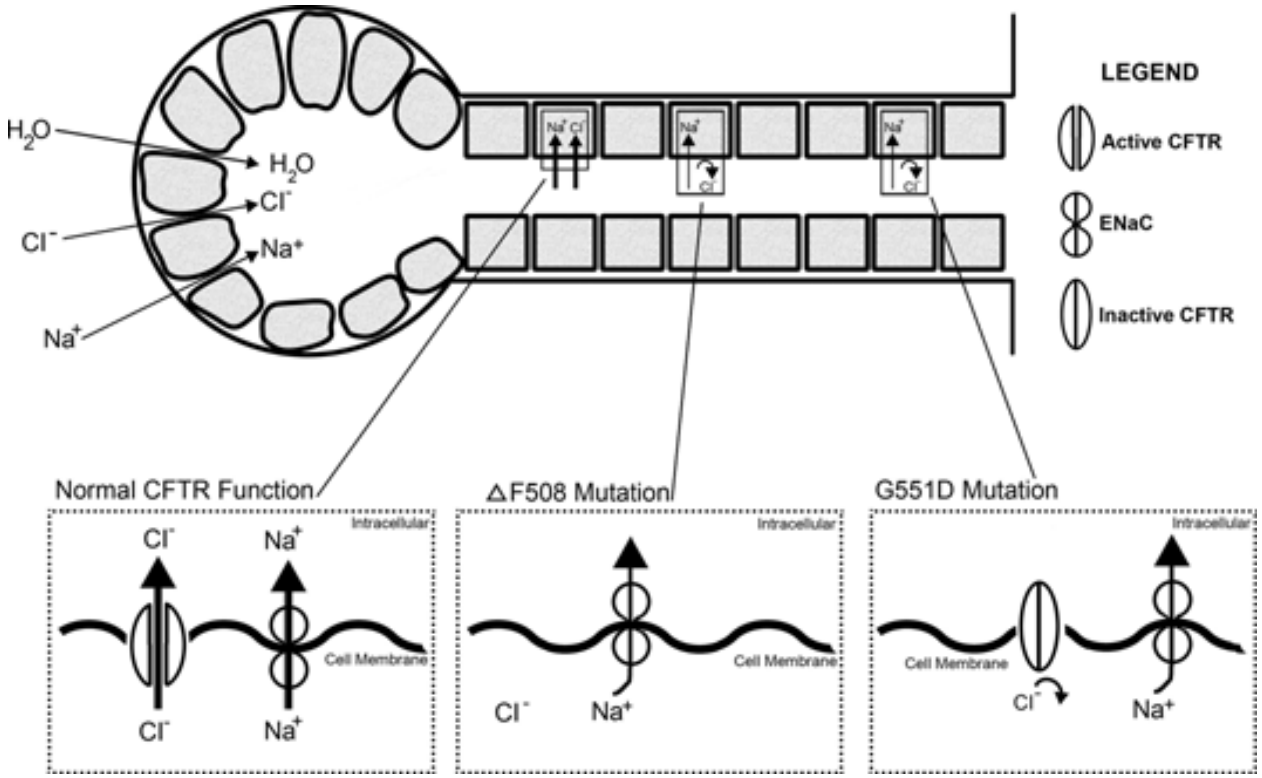


- Defective CFTR (mutations in *CFTR* gene); incidence- 1:3000 in Caucasians
- CF is characterized by viscous secretions that affect exocrine glands: lungs and pancreas
- Diagnosis:
  - Clinical presentation: symptoms, a positive family hx, NBS or prenatal testing

AND

  - Laboratory testing for CFTR dysfunction: positive sweat test or identification of two CF-causing mutations

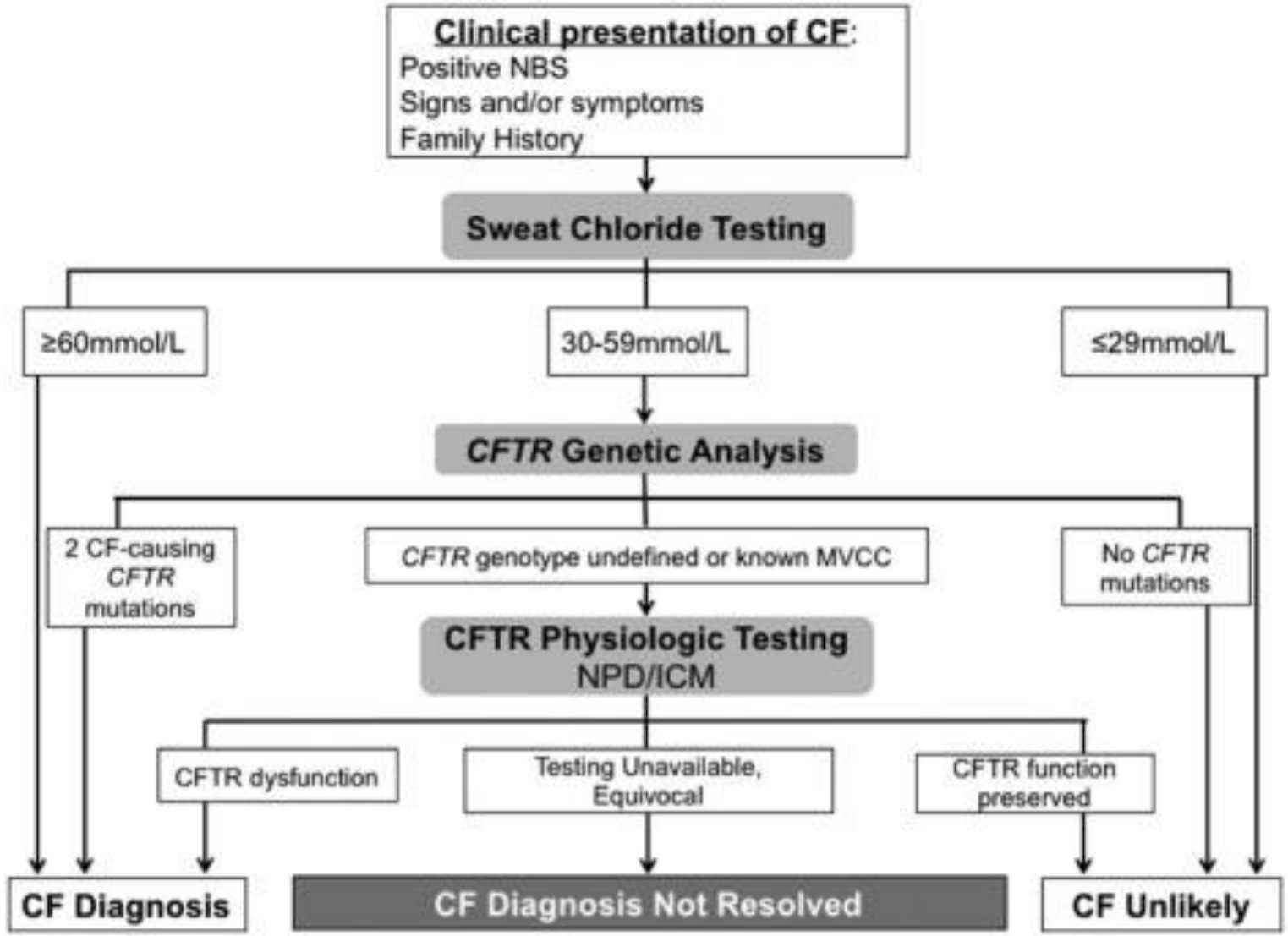
Dysfunctional CFTR causes elevated sweat chloride



Collie et al.,Pediatric Pulmonol. 2013

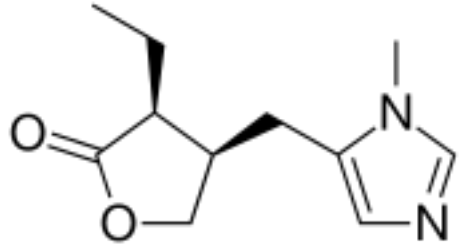
1948 New York Heat Wave

Dr. Paul di Sant'Agnese



Farrell et al., J Pediatr. 2017

Sweat testing methodology



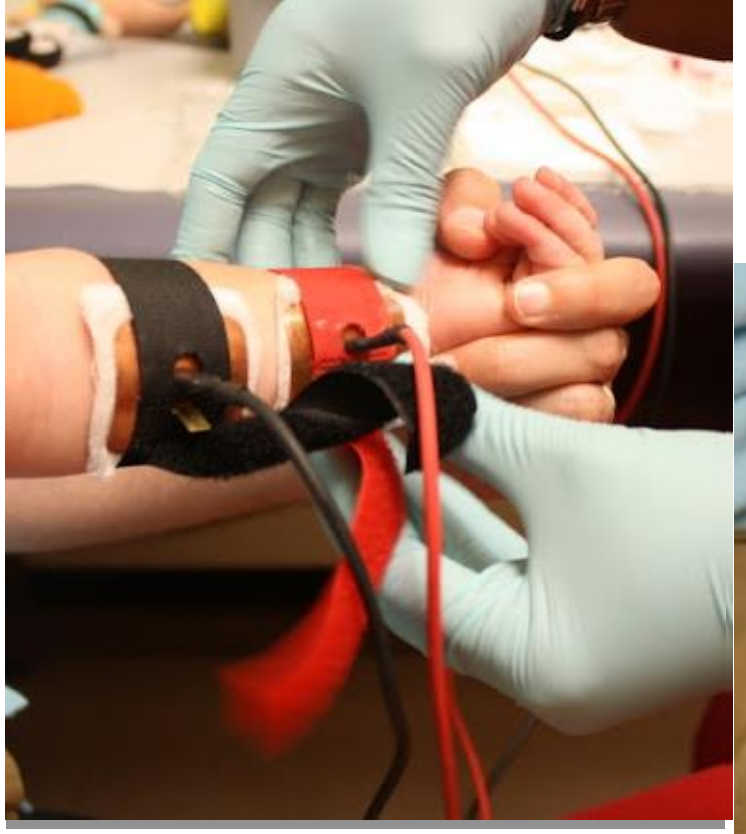
- Sweat collection stimulated by pilocarpine iontophoresis and collected into either a gauze, filter paper or coiled tubing.

- Quantitative sweat chloride measurement by coulometry:
  - ≤ 29 mmol/L = CF unlikely
  - 30 to 59 mmol/L= intermediate
  - ≥ 60 mmol/L = indicative of CF

Farrell et al. J Pediatr 2017;181:S4–15.

Gibson and Cooke (Gauze) Method

Gibson and Cooke, Pediatrics 1959



Wescor Macroduct Method

1983

CF Foundation Guidelines

- Follow CLSI C34 4th ed. procedures for sweat collection and analysis
- Min age for testing: 48 hours (symptomatic)
  - Asymptomatic newborns- >10 days old
- Sweat collection and analysis performed in duplicate
- Insufficient collection (QNS), if individual site <75 mg or < 15 uL
  - Samples should not be pooled (requirement based on physiologic sweat rate of >1 g/m²/min for standard electrode size, stimulation area and collection time)
- QNS samples should be ≤ 10% for 6 weeks- 3 months and ≤ 5% in patients > 3 months of age

No recommendations or guidelines on how to achieve these QNS rates

Farrell et al., J Pediatr. 2017

CHM.30150 Sweat Rejection Incidence Rate **Phase I**

The incidence of insufficient sweat samples is routinely monitored.

NOTE: For quality monitoring, laboratories must collect data on the number of patients from whom an insufficient sweat sample has been obtained (QNS - quantity not sufficient). For patients older than three months of age, the annual insufficient rate should not exceed 5%. For patients six weeks to three months of age, the rate should not exceed 10%. For patients less than six weeks of age, an acceptable rate has not been determined. If these rates are exceeded, the collection procedure should be reevaluated for consistency with the CLSI guideline C34 4th ed. The most common cause of insufficient samples is the use of inappropriate collection devices (see CHM.29850).

For bilateral sweat collections, a QNS patient is a patient with an insufficient sample collected from both sites (eg, right arm and left arm). Each patient encounter is counted to determine the total number of sweat collections; thus, the same patient may appear repeatedly in the total population as well as the QNS population.

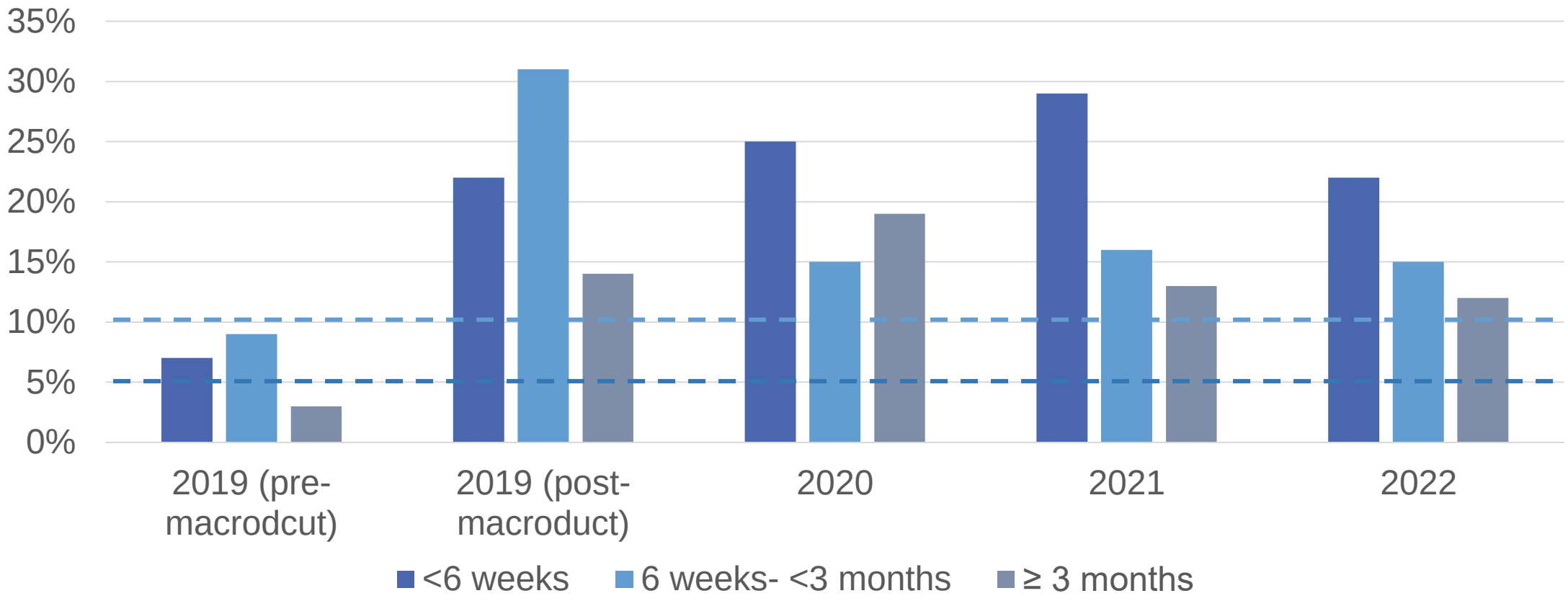
Evidence of Compliance:

- ✓ Records of insufficient collection **AND**
- ✓ Records of corrective action if rate exceeds the norm

Challenges with QNS

	Study population	Gibson-Cooke gauze/ filter paper QNS %	Macroduct QNS%
Hammond et al., J Pediatr 1994	1090 all ages	0.7%	**6.1%**
Mastella et al., 2000	318 all ages	3.6%	**9.1%**
Kleyn et al., 2011	315 infants	17%	**21%**
Laguna et al., 2012	568 infants (<1 yr)	**15.4%**	2.1%
Aqil et al., 2014	269 all ages		**16.7%** ≤3 mo (n=42) **9.3%** >3 mo (n=227)
Suh-Lailam et al., 2019	269 all ages		**21%** ≤3 mo (n=116) **11%** >3 mo (n=153)

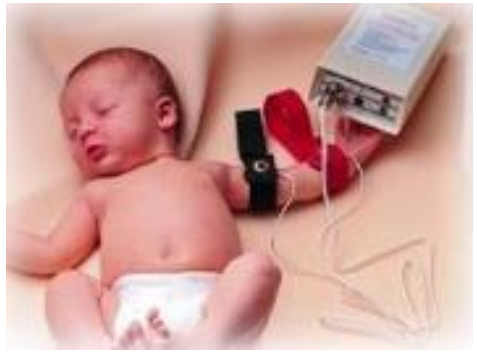
Challenges with QNS: our experience



Where problems can arise

1. Preanalytical

- Medication
- Illness
- Nutritional/Hydration status
- Physical maturity



2. Technical / procedural

- Collection sites and timing
- Poor contact of pilogels with arm
- Collector not placed on arm with proper pressure/location
- Collector not secured (patient removed/moved)
- Poor harvesting

Preanalytical risk factors

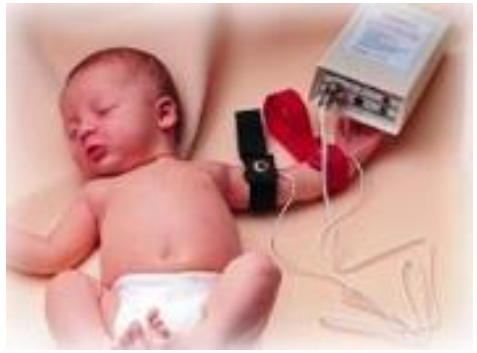
Patient Risk Factors for QNS	Recommendations/ interventions
Patient age and weight	Delay testing in infants <2kg, <10 days or <37 weeks gestation
Hydration Status	Provide patient instructions, helpful to suggest feeding infant hour prior to testing
Medications	Topiramate and mineralocorticoids can reduce sweating
Illness	Reschedule testing if patient has a fever or GI symptoms

QNS rates in inpatients vs. outpatients

	Inpatient QNS	Outpatient QNS
Total	**32% (86)**	**13% (725)**
Age group:		
<6 weeks	40% (10)	20% (211)
6 weeks- <3 months	8.3% (12)	13% (86)
>/= 3 months	36% (64)	8.1% (492)

Where problems can arise

1. **Preanalytical**
   - Medication
   - Illness
   - Nutritional/Hydration status
   - Physical maturity

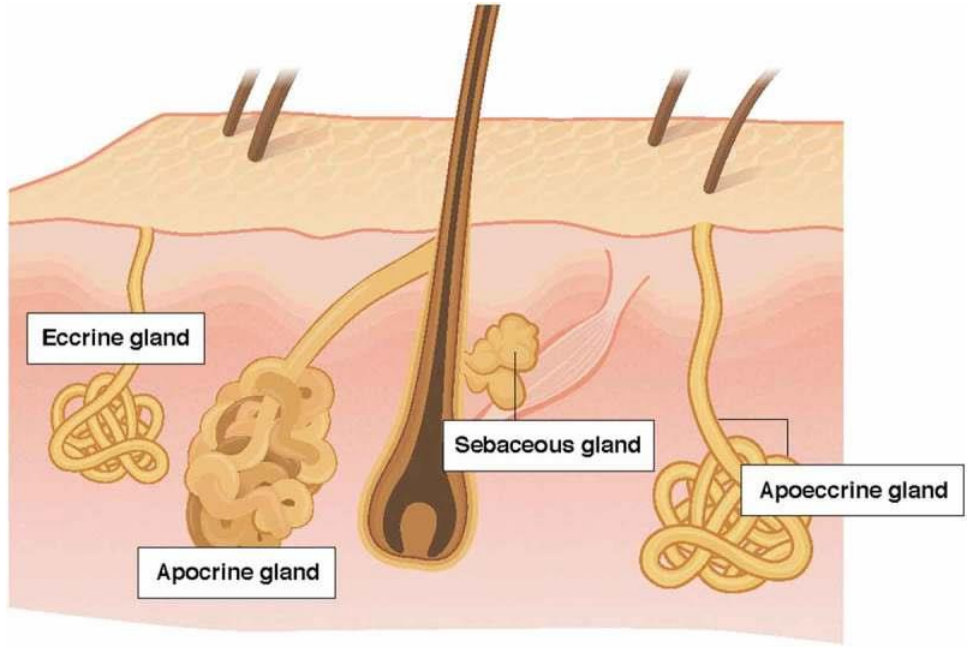


2. **Technical / procedural**
   - Collection sites and timing
   - Poor contact of pilogels with arm during stimulation
   - Poor contact of collector with arm during collection
   - Poor harvesting

Sweat collection site- does it matter?

Eccrine vs. apocrine sweat glands

- Pilocarpine acts on the muscarinic receptors of the eccrine sweat glands.
- Sweat composition of eccrine and apocrine glands is different; therefore, results may not be interchangeable

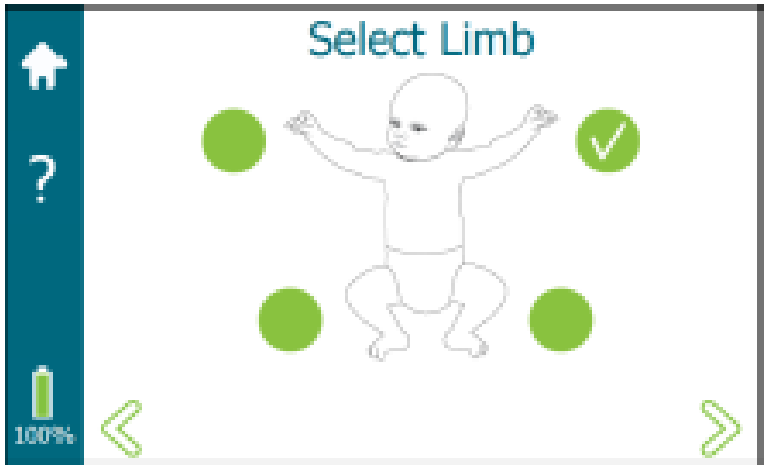


Lower arm is preferred site, especially for infants (CLSI C34).

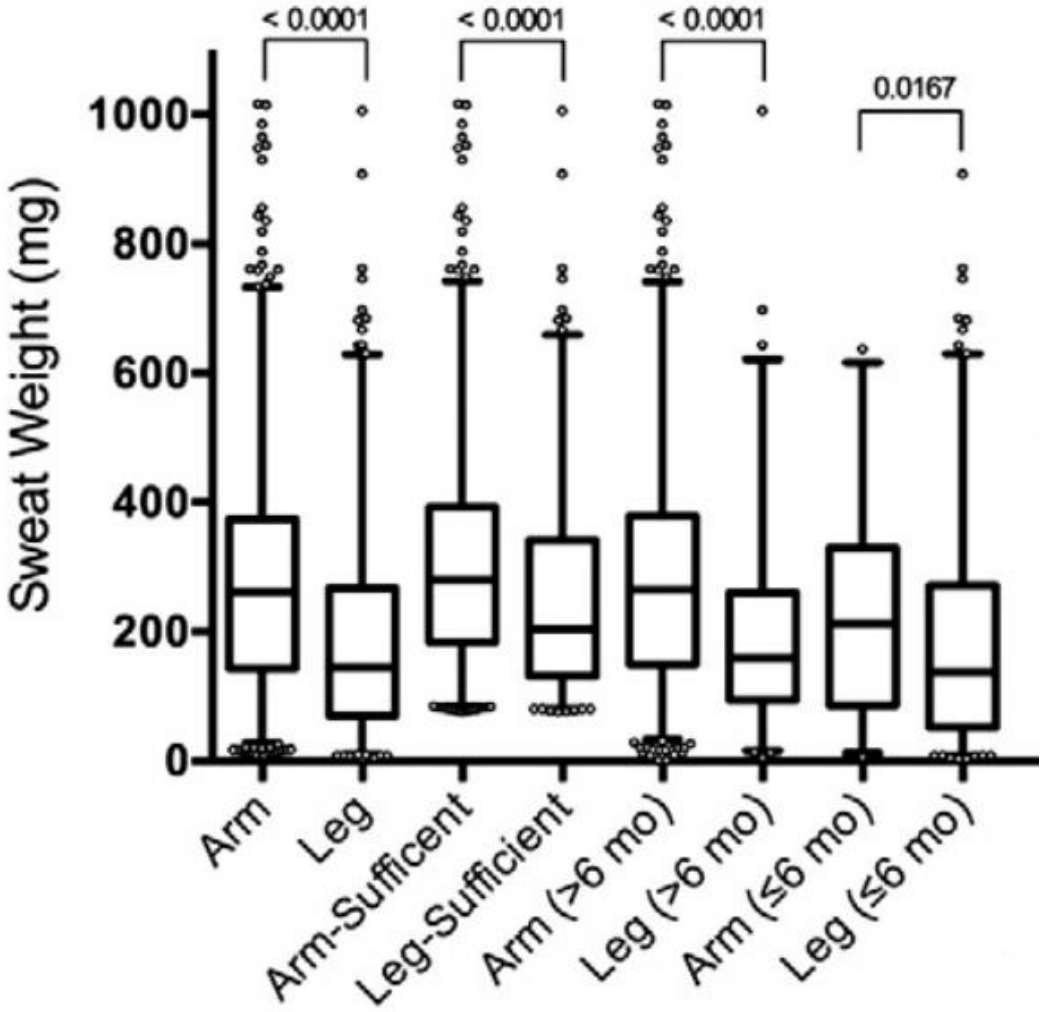
Baker et al., Eur J Appl Physiol. 2020

Sweat collection sites – does it matter?

	One Leg	Both Arms	Both Legs
QNS % (n)	15.8% (19)	16.5 % (762)	0% (1)
	Collection events:	**Legs**	**Arms**
	QNS % (n)	60% (20)	23% (1542)



Sweat collection sites – does it matter?



Arms n= 781
Legs n= 458

DeMarco et al., Clin Biochem. 2015

What about timing for sweat collection?

- Minimum requirement is from 1963 study that establishes a needed sweat rate of 1 g/m^2/ min = 75 mg or 15 uL over 30 minutes using a 2x2 collection area.
  - Study of 29 individuals, where electrolyte concentrations were greater at higher sweat rates.

Recommended that 30 min timer be started once sweat (blue dye) is visible in the collection device. If no sweat is visible, 30 min timer is started after 5 minutes.

Gibson and Disant Agnese, J Pediar 1963

Can the minimum sweat weight/ volume requirement be lowered?

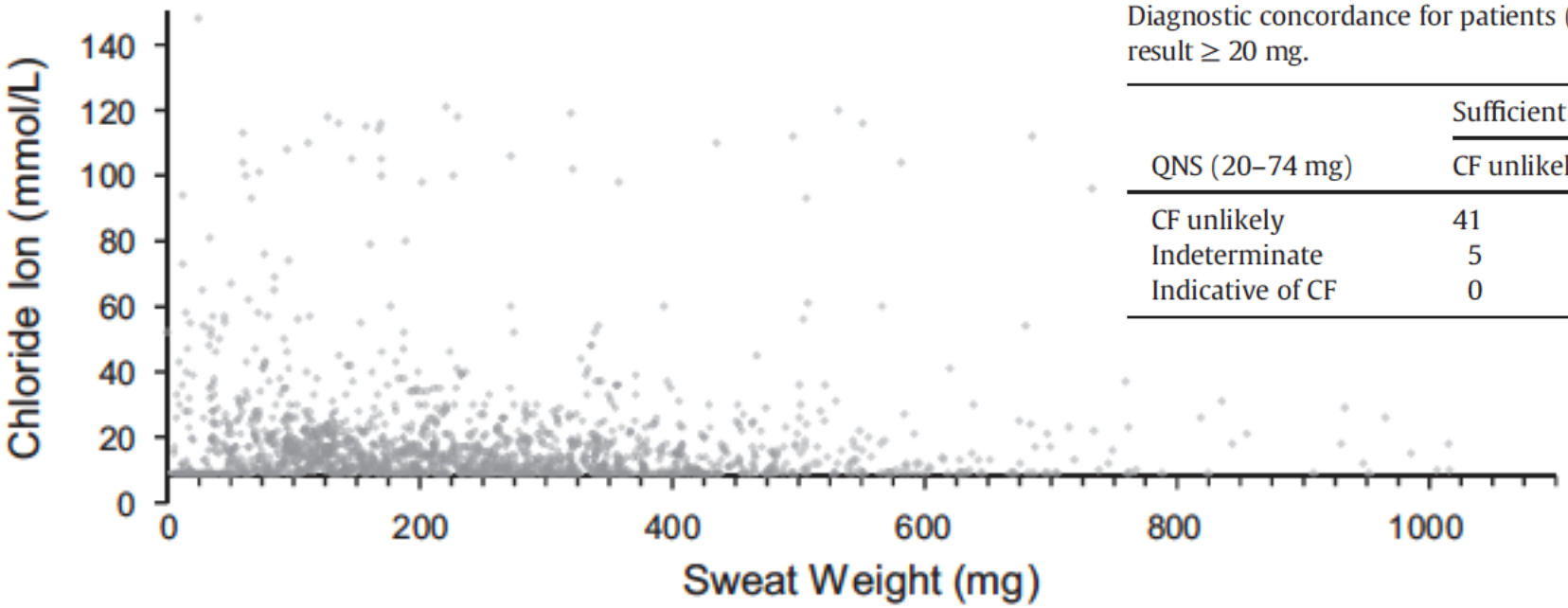
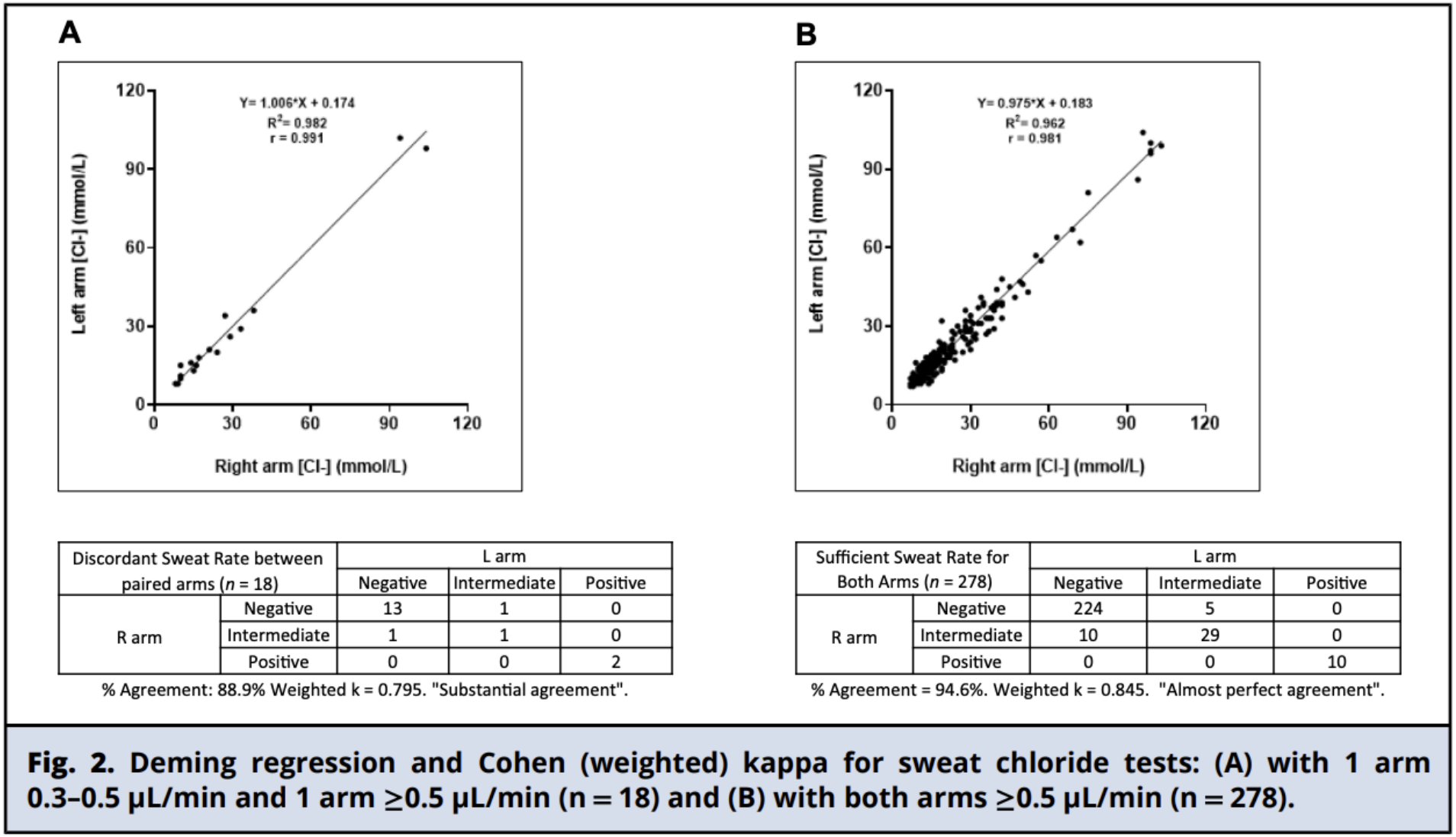


Table 2
Diagnostic concordance for patients (n = 60) with at least one sufficient and one QNS result ≥ 20 mg.

	Sufficient collection (≥75 mg)		
QNS (20–74 mg)	CF unlikely	Indeterminate	Indicative of CF
CF unlikely	41	4	0
Indeterminate	5	3	0
Indicative of CF	0	0	7

n=1348, no correlation between sweat weight and chloride concentration (r = -.06)

DeMarco et al., Clin Biochem. 2015



Discordant Sweat Rate between paired arms (n = 18)		L arm		
		Negative	Intermediate	Positive
R arm	Negative	13	1	0
	Intermediate	1	1	0
	Positive	0	0	2

% Agreement: 88.9% Weighted k = 0.795. "Substantial agreement".

Sufficient Sweat Rate for Both Arms (n = 278)		L arm		
		Negative	Intermediate	Positive
R arm	Negative	224	5	0
	Intermediate	10	29	0
	Positive	0	0	10

% Agreement = 94.6%. Weighted k = 0.845. "Almost perfect agreement".

Fig. 2. Deming regression and Cohen (weighted) kappa for sweat chloride tests: (A) with 1 arm 0.3–0.5 µL/min and 1 arm ≥0.5 µL/min (n = 18) and (B) with both arms ≥0.5 µL/min (n = 278).

Omosule et al., JALM. 2023

Common Interventions

Preanalytical

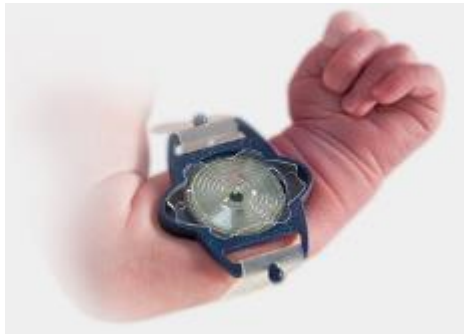
- Providing water to patients
- Excluding patients on IV fluids
- Deferring patients on mineralocorticoids
- Blanket warmers to wrap patients
- Using temperature-controlled rooms for sweat collection
- Hot pack secured with parafilm

Technical

- Eliminating sweat collections from areas other than forearm
- **Retraining staff members frequently and limiting # of collectors**
- **Regularly examining QNS collections**

Newer collection system: Macroduct Advanced

- Inducer has a step-by-step LCD touchscreen to time and guide all aspects of testing
- Changes to macroduct collection device
  - Visual indicators (marks) of collection volume on the collector tubing
  - Elliptical shape gives better fit for small arms



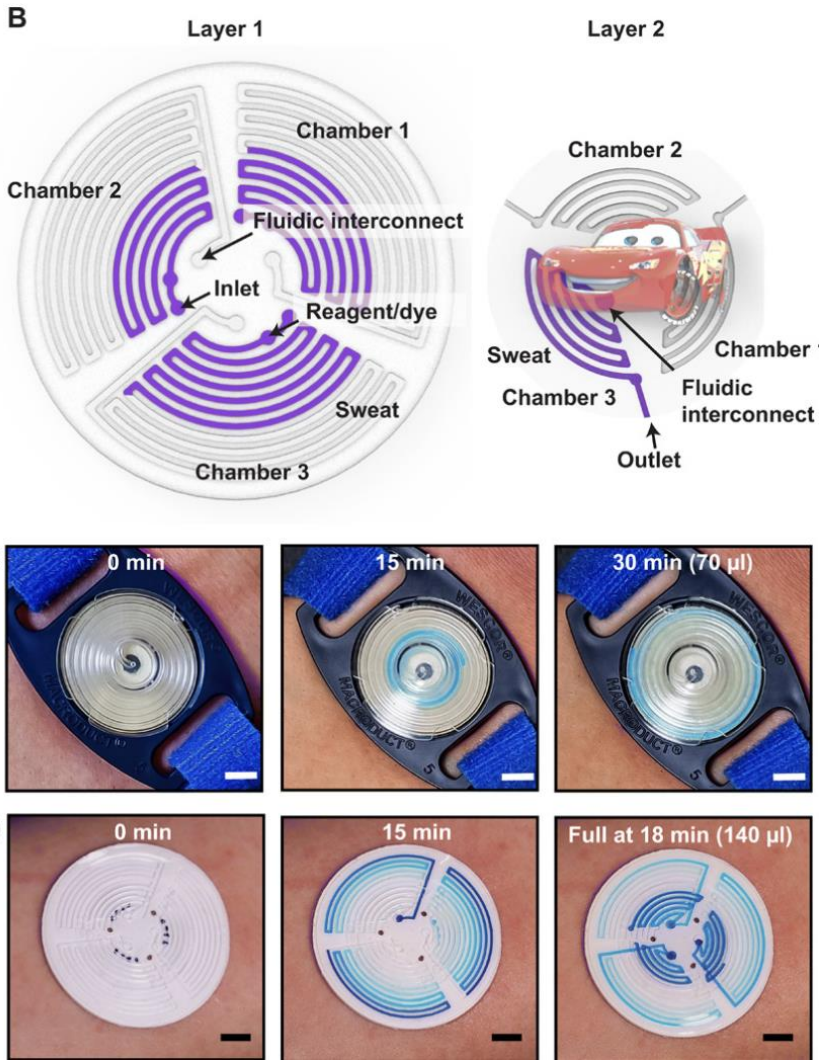
Vs.

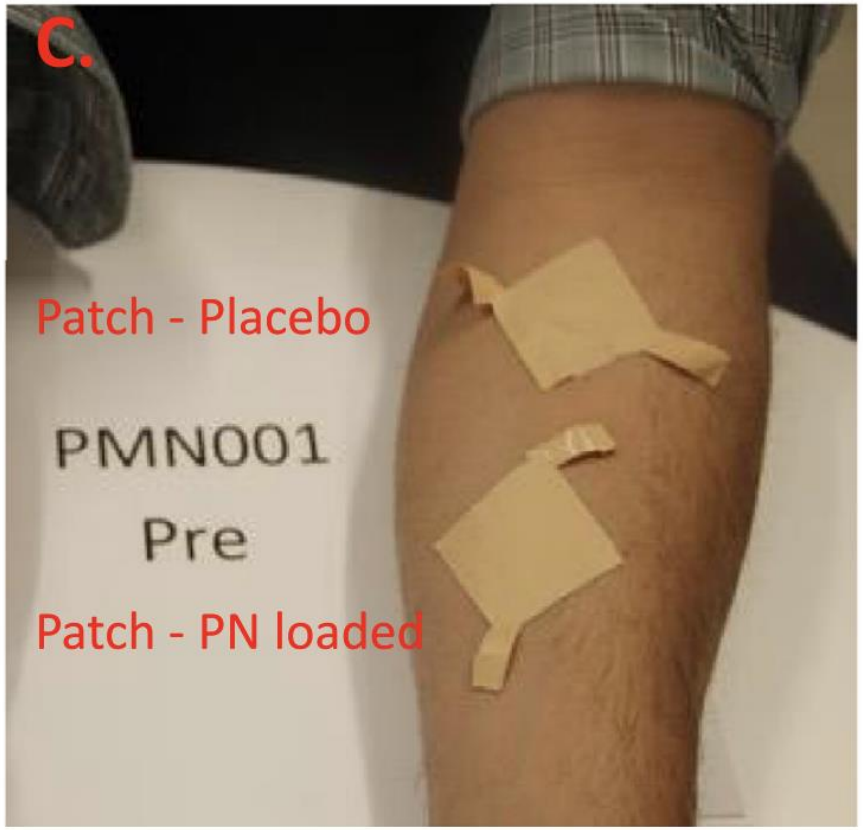
Other ongoing work

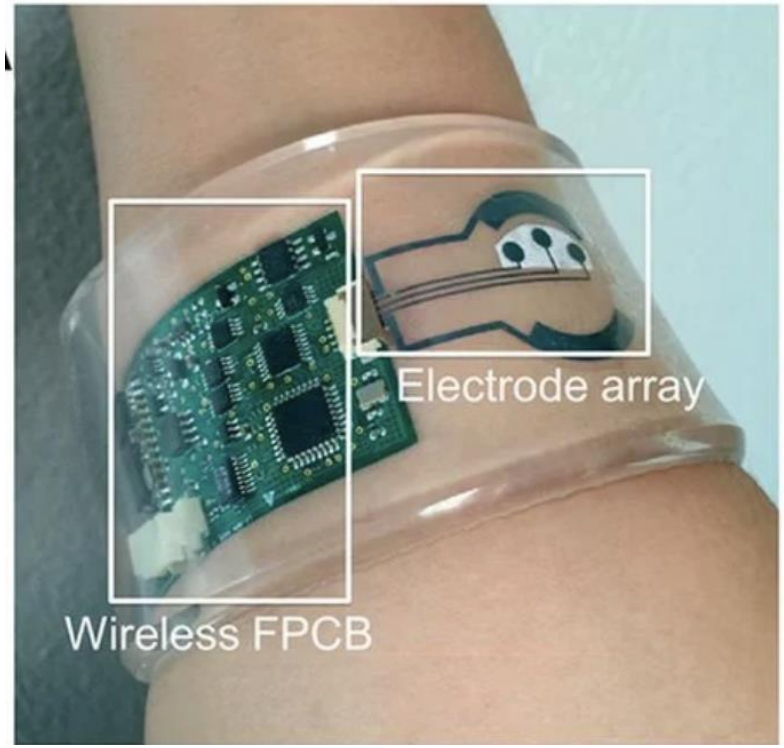
- Vendor provided training and assessment of our current protocol
  - Key findings:
    - Waiting 10 minutes for first appearance of sweat in the coil to start 30-minute timer (compared to 5 min previously).
    - Slowly engaging the plunger to push sweat out into collection tube to avoid loss of sample
    - Using a surgical clamp on the end of the collection tube before taking off the end of the coil to avoid sweat loss
- Working with CF clinic to define criteria for inpatient and outpatient sweat collecitons
  - Age, weight
  - Previous QNS history

Conclusions

- Obtaining sufficient sweat volumes remains a challenge for many CF centers.
- There are several preanalytical and technical factors that can influence successful sweat collection in children.
  - Evidence to support restricting sweat collections to forearms as well as ensuring patient is healthy and appropriate size and age.
  - Continual training and education of staff
- Detailed analysis of QNS rates and providing better clinical decision for placing sweat test orders can be key drivers of success







Ray et al., Sci Transl Med 2021
Chen et al., J Cyst Fibros 2023
Emaminejad et al., PNAS 2017

Thank you!

- Quality Specialists
  - Brittany Chiodo
  - Vivian Whitner
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  - Izmarie Poventud-Fuentes
  - Daisy Unsihuay
  - Kaitlyn Bolte
  - Linh Nguyen
- CF Clinic
  - Clement Ren
  - Lisa Young

Questions?

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Blood Lead Testing in Children

Tracey Polsky, MD PhD

March 6, 2024

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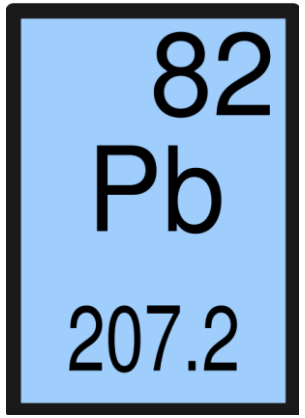
Learning Objectives

- Understand the critical role of lead screening in pediatric populations.
- Discuss the implications of the updated blood reference value on pediatric health care.
- Develop strategies to enhance lead testing, considering local conditions and patient needs.

Epidemiology of Lead Exposure

What is Lead?



- Lead is a heavy metal that is naturally occurring in our environment (air, soil, water).
- Exposure comes from human activities (leaded gasoline, lead-based paint).
- Lead is absorbed into the body via inhalation or ingestion.
- Multiple sources of lead found in and around our homes.

- Lead has no biologic role in our body - any detectable lead level is abnormal.

Common Sources of Lead Exposure

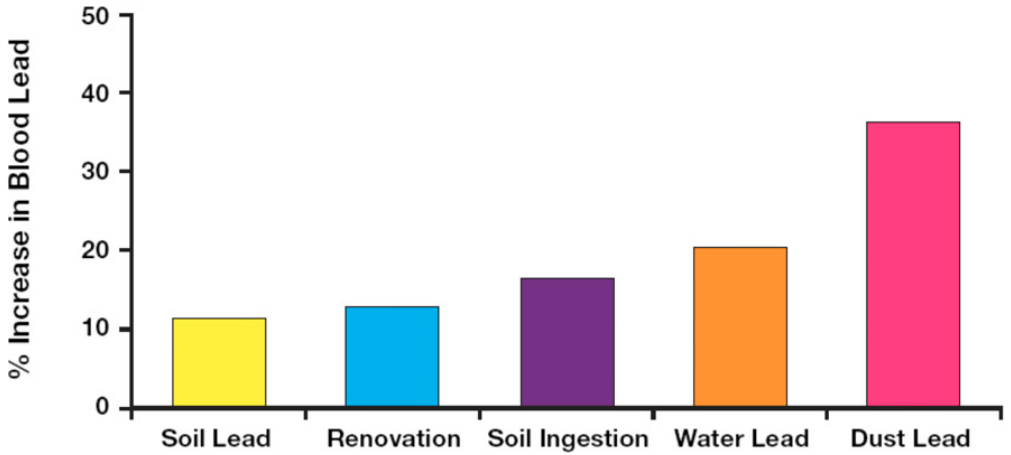
- Before the 1980's, the main source of lead exposure across all ages was aerosolized lead from leaded gasoline.
- **The primary source of elevated blood levels in U.S. children is from lead-based paint, which creates lead paint-contaminated house dust and lead-contaminated soil.**
- The remaining cases can be attributed to contaminated drinking water and imported goods (candies, spices, pottery, herbal remedies).
- Risk factors for lead poisoning include age younger than 5 years, low socioeconomic status, living in housing built before 1978, and use of imported food/medicine/pottery.

Common Sources of Lead Exposure

Source	Comment
House paint used before 1978 but especially before 1960	Deteriorated paint releases fine lead dust during home renovation.
Toys and furniture painted before 1976	
Painted toys made outside the United States	
Lead bullets, fishing sinkers, certain weights	Exposures often occur during practice in firing ranges.
Plumbing, pipes, and faucets	Lead leaches into drinking water when the pipes are connected with lead solder.
Especially plumbing installed before 1986	
Soil contaminated by lead	Often in soil near highways and in yard of houses with exterior lead paint.
Hobbies involving soldering such as stained glass, jewelry making, pottery glazing, and miniature lead figures	Always check the labels.
Children's paint sets and art supplies	Always check the labels.
Pewter pitchers and ceramic dinner ware	
Storage batteries	
Parental occupation	Auto repair, mining, battery manufacture, pipe fitting and plumbing, welding, firing range use, ship building, painting, construction.
Folk remedies	Greta and Azarcon, Hispanic traditional medicines; Ghasard, an Indian folk medicine; and Ba-baw-saw, a Chinese herbal remedy, contain lead.
Cosmetics	Examples include Swad brand Sindoor, a cosmetic product used by traditional Hindus; Tiro, an eye cosmetic from Nigeria.
Candy from Mexico	Ingredient tamarind may contain lead.
Toy jewelry	A child died in 2006 after swallowing a metal heart charm that came with a purchase of shoes made by Reebok.

AAP council on Environmental Health. Pediatrics, 2016

Contribution of lead exposure to children's blood lead concentrations



The major source of lead is paint but ingestions of house dust and soil are the major pathways of exposure

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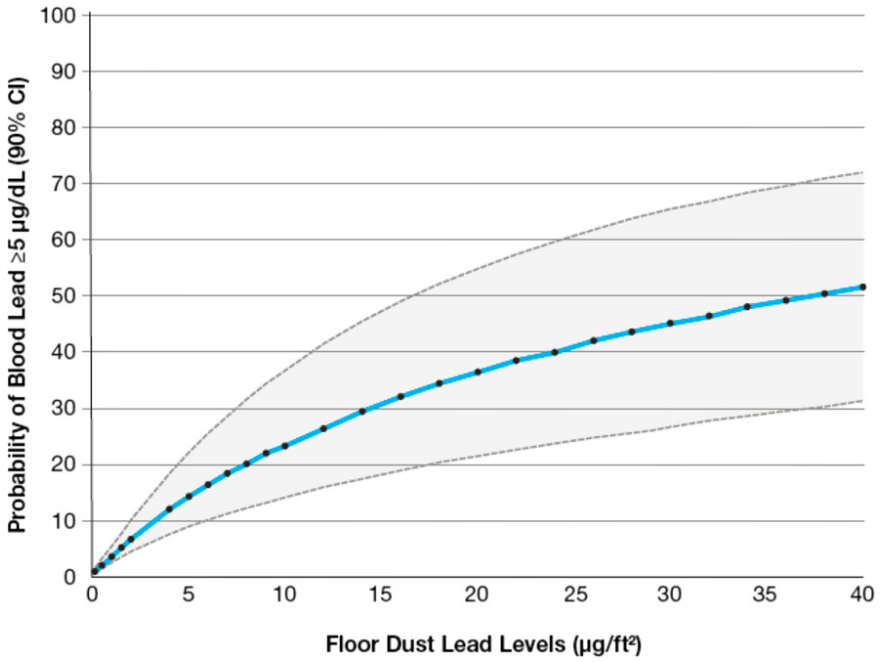
Lead in House Paint

- Lead use in paint began during colonial times and peaked in the 1920s.
- Lead was added to paint to accelerate drying, increase durability, and resist moisture.
- Bright white, tastes sweet.
- 1977: Lead paint banned in residential properties and public buildings.



Children living in pre-1978 housing

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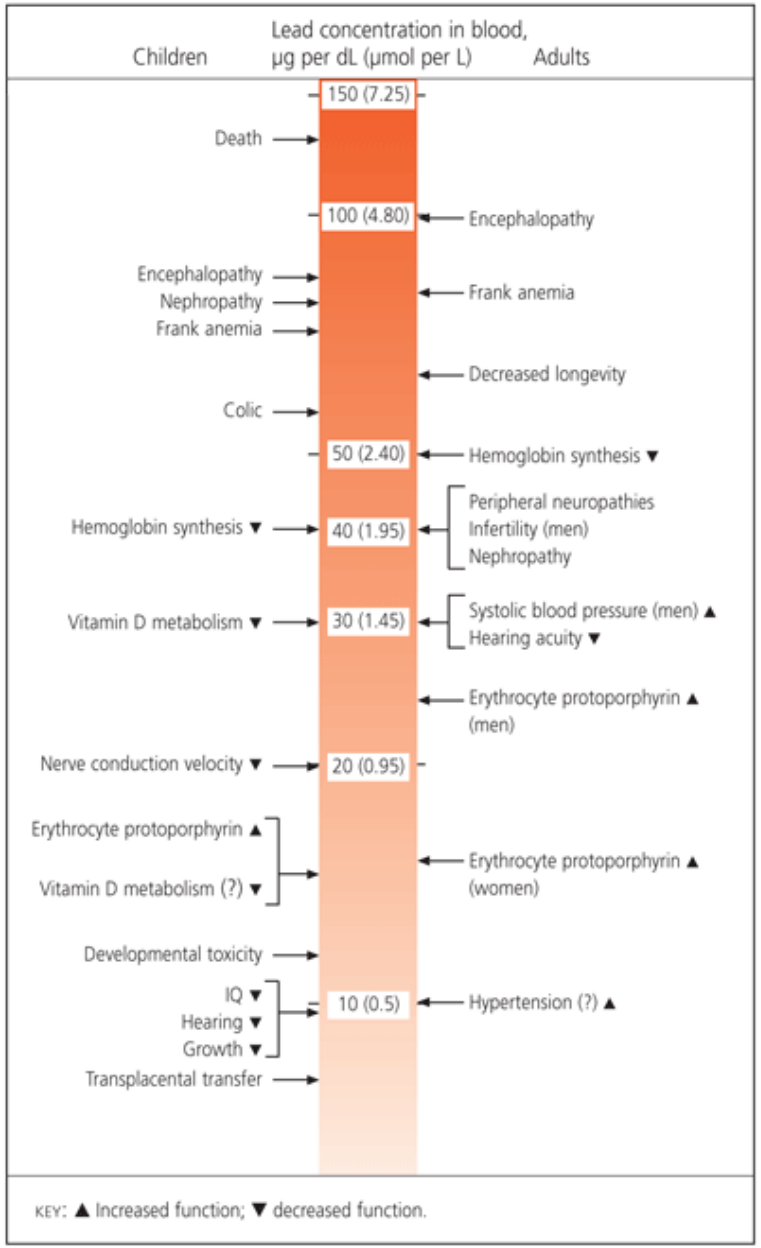
AAP council on Environmental Health. Pediatrics, 2016

Lead Exposure is a Pediatric Problem

- Young children (less than 5 years old) are at highest risk of lead poisoning.
- Growing bodies absorb more lead than adults and have more sensitive brains and nervous systems.
- Engage in age-appropriate hand to mouth behavior, which results in lead and lead dust ingestion.
- Iron deficiency is a risk factor for lead toxicity.

Symptoms of Lead Poisoning

- Lead poisoning is often asymptomatic (but the effects are irreversible).
- Even very low levels (<5 ug/dL) are associated with impaired neurocognitive and behavioral development.
- Nonspecific symptoms occur at higher levels.
- Very high levels can cause vomiting, convulsions, encephalopathy, and death.



What is a Normal Blood Lead Level (BLL)?

- There is no normal or safe blood lead level.
- CDC definition of elevated BLL has evolved over time.
- 2012*: CDC replaced "blood lead level of concern" with "blood lead reference value (**BLRV**)."
- Statistical measure: based on the 97.5th percentile of blood lead distribution in children aged 1-5 years.

1985: "Elevated Blood Lead Level", > 25 ug/dL

1991: "Level of concern", > 10 ug/dL

*2012: BLRV, > 5 ug/dL

2021: BLRV, > 3.5 ug/dL

CDC will update the BLRV every 4 years

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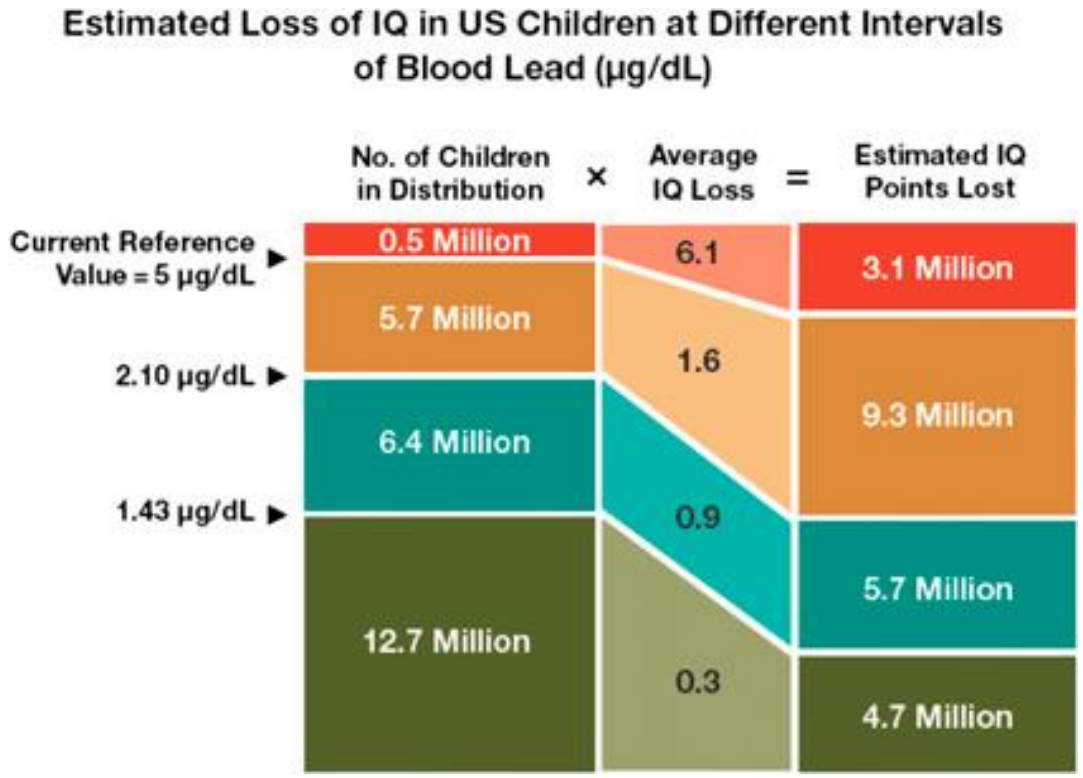
Blood Lead Reference Value (BLRV)

- The BLRV is not a measure of toxic vs non-toxic.
- Children with levels >BLRV are among the top 2.5% of U.S. children with the highest blood levels.
- Lowering of the BLRV facilitates earlier intervention and identification of high risk children.



AAP council on Environmental Health. Pediatrics, 2016

Over 500,000 U.S. children are estimated to have blood lead levels > BLRV

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Lead Poisoning Prevention

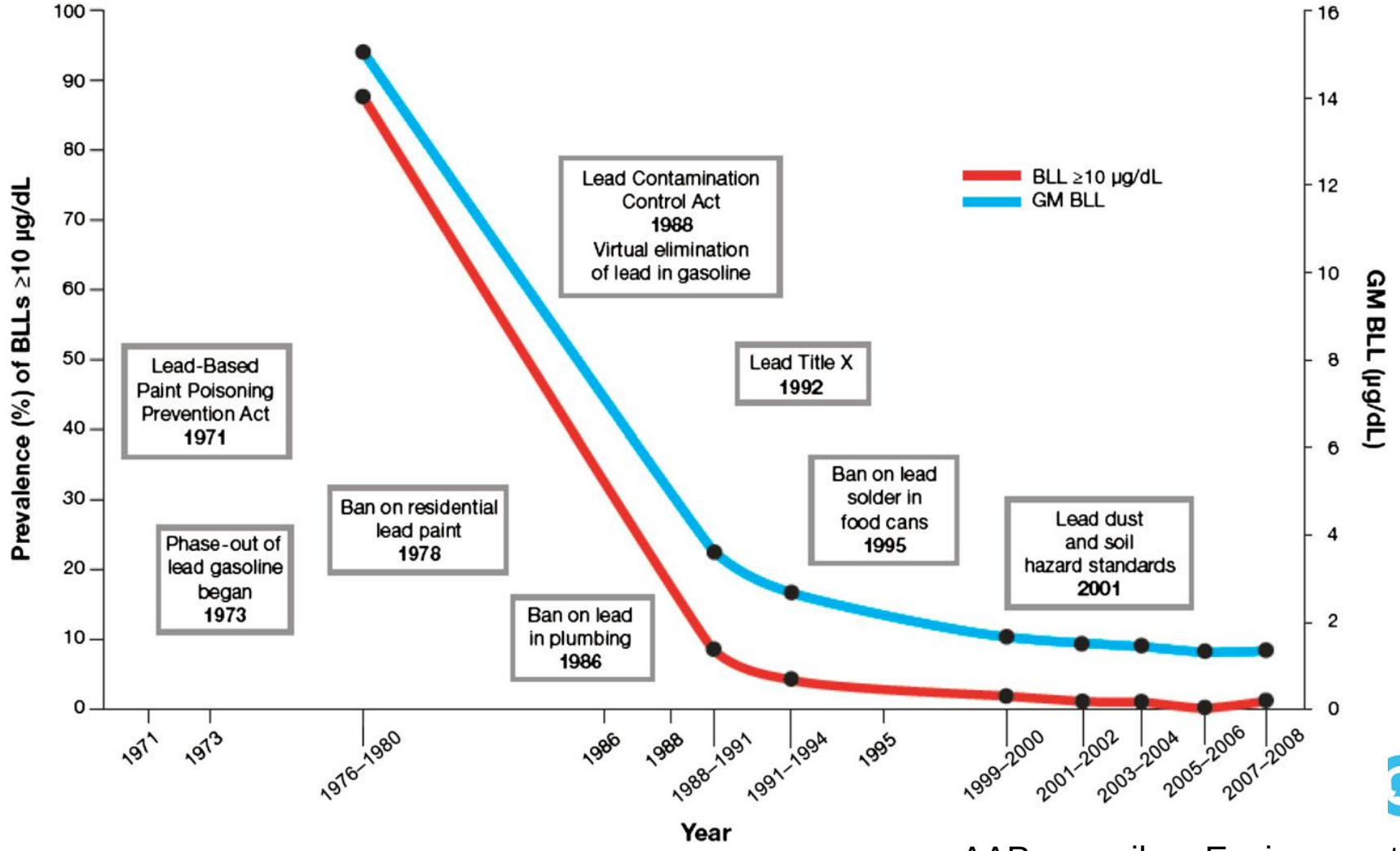
- Deleterious effects of lead on neurocognitive and behavioral development are irreversible (even at very low levels).

- **Primary prevention: removal of lead risks from the environment before exposure (programs, laws and education).**

- Secondary prevention: removing the source of lead exposure and prevent further harm once an elevated lead level is detected (screening and case management).

Primary Prevention of Lead Exposure is Key

Primary prevention is the most reliable and cost-effective measure to protect children



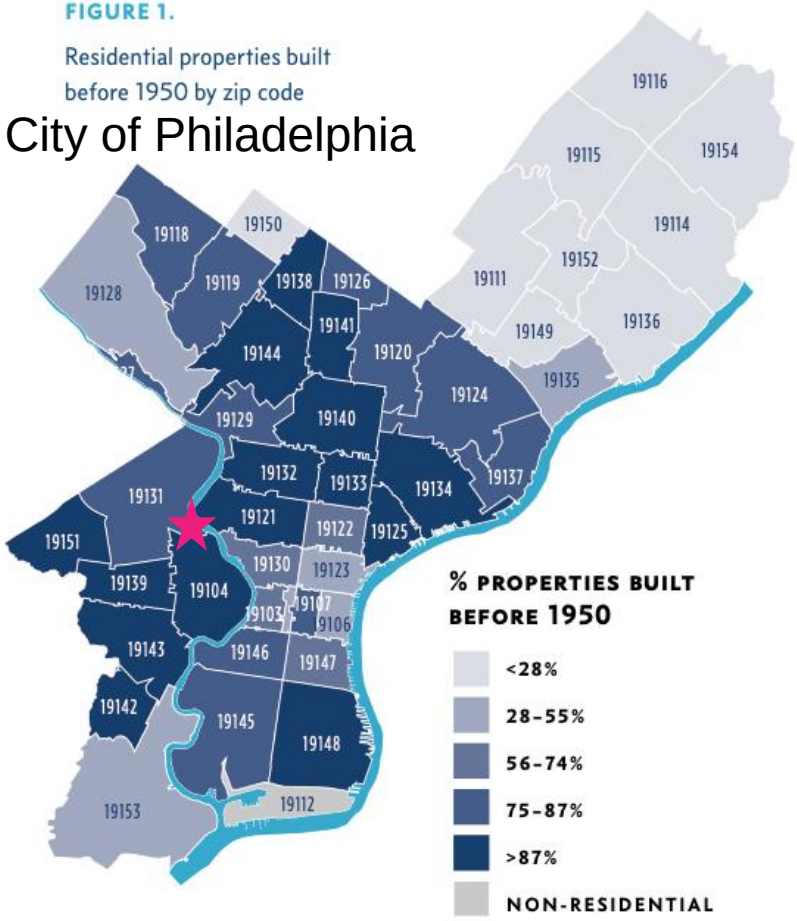
AAP council on Environmental Health. Pediatrics, 2016

Continued Importance of Prevention

FIGURE 1.

Residential properties built before 1950 by zip code

City of Philadelphia



Current as of 2017

WanaBana apple-cinnamon fruit purée pouches were among three products made in a plant in Ecuador that were found last year to be contaminated with lead.

Lead-Tainted Applesauce Sailed Through Gaps in Food-Safety System

Hundreds of American children were poisoned last year. Records show how, time and again, the contamination went unnoticed.

Feb 27, 2024

April 2014

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Guidelines for Lead Screening

CDC recommendation: cities and states should target communities with the highest risk of lead exposure.

CMS requirements: all Medicaid enrolled children at ages 12 months and 24 months, or 24-72 months if no previous.

Universal screening for high-risk areas.

Lead Poisoning Screening Criteria

Screen children who meet any of the following criteria:

All Medicaid-enrolled or -eligible children at 12 months and 24 months of age

All children who are identified as high risk based on results of a personal risk questionnaire (if one of the following questions is answered "Yes" or "Don't know"):

- Does your child live in or regularly visit a house that was built before 1950 (this could apply to a home day care center or the home of a babysitter or relative)?
- Does your child live in or regularly visit a house built before 1978 with recent or ongoing renovations or remodeling (i.e., within the past six months)?
- Does your child have a sibling or playmate who has or has had lead poisoning?

All refugees, recent immigrants, and international adoptees on arrival in the United States; repeat screening three to six months later for children six months to six years

All children who are identified to be at increased risk by the Centers for Disease Control and Prevention's state or local screening recommendations (i.e., high-risk zip codes)

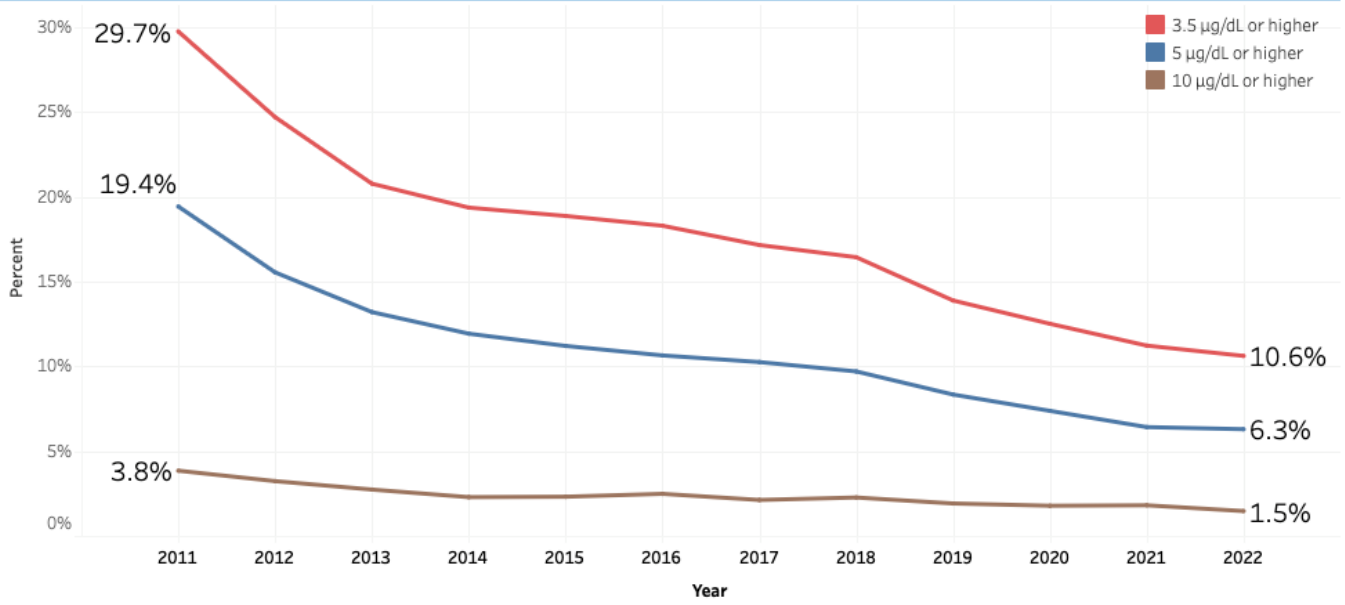
Adapted with permission from Warniment C, Tsang K, Galazka SS. Lead poisoning in children. Am Fam Physician. *2010;81(6):753.*

Mayans, L. AAFP. Lead Poisoning in Children, 2019.

Decline of Lead Exposure in Philadelphia Children

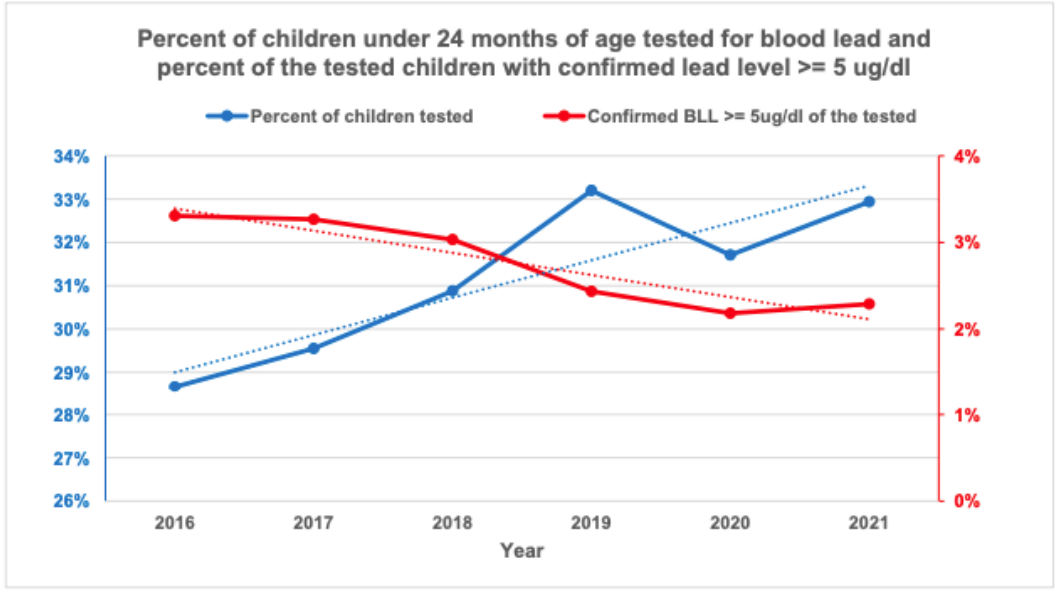
Lead exposure among children has become less common. In 2011, about 30% of screened three-year-olds **ever** had an elevated blood lead test of 3.5 µg/dL+ (red line) at some point in their lifetime. In 2022, this declined to about 11%. About 6% of three-year-olds ever had an elevated blood lead test of 5 µg/dL+ (blue line) in 2022, down from 19% in 2011. About 4% of three-year-olds in 2011 ever had an elevated blood lead test of 10 µg/dL+ (brown line) compared to 1.5% in 2022.

Percent of screened three-year-olds who ever tested positive for elevated blood lead levels at some point in their lifetime, 2011-2022



Source: Pennsylvania Department of Health.
Note: The Health Department's threshold for blood lead levels to be considered "elevated" is 3.5ug/dL. Prior to 2020, this threshold was 5 ug/dL. A blood lead level of 10 ug/dL or higher is considered very high.

www.Phila.gov



PA DOH

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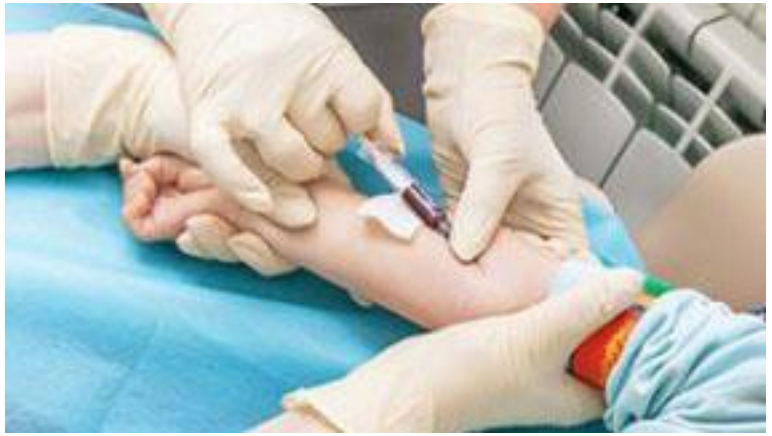
Laboratory Evaluation of Blood Lead

Pre-analytical Considerations: Sample Types

- Most common sample type is anticoagulated whole blood.
- Serum/plasma are not preferred because circulating lead is predominantly associated with red blood cells.
- Two types of blood collections
  - Capillary sample: a finger-prick or heel-prick is used to take a small amount of blood
  - Venous sample: venous phlebotomy



Images from CDC.gov

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Pre-analytical Considerations: Collection Tubes

- Preferred tube types
  - Royal blue (K2EDTA or NaHep): metal-free tube used for trace element, toxicology, and nutritional studies
  - Tan (K2EDTA): lead free tubes used for lead testing

- Acceptable for capillary samples
  - Lavendar top (K2EDTA): available in microtainer size for capillary collection, not certified trace metal or lead free

Blood Lead Level: Screening Versus Confirmation

- Benefit to a capillary sample is ease of draw and better workflow in the primary care setting.
- External contamination is a concern with capillary samples.
- Capillary blood specimens with elevated lead levels (> BLRV) should be confirmed with a venous specimen.
- Consideration for pediatrics: sample sharing.

Recommended Schedule for Obtaining a Confirmatory Venous Sample

Capillary Blood Lead Level (µg/dL)	Time to Confirmation Testing
≥3.5–9	Within 3 months
10–19	Within 1 month
20–44	Within 2 weeks
≥45	Within 48 hours

CDC.gov

The higher the capillary screening BLL,
the more urgent to confirm with a venous sample.

Analytical Considerations: Methodologies

- Gold standard methods: Inductively Coupled Plasma/Mass Spectrometry (ICP/MS) or Atomic Absorption Spectrometry (AAS)
  - Can only be performed in a highly complex clinical laboratory
  - Can be used for screening or for confirmatory testing (capillary or venous samples)

- Point-of-care testing: Anodic Stripping Voltammetry (ASV)
  - LeadCare instruments
  - Can only be used for screening (capillary samples only)

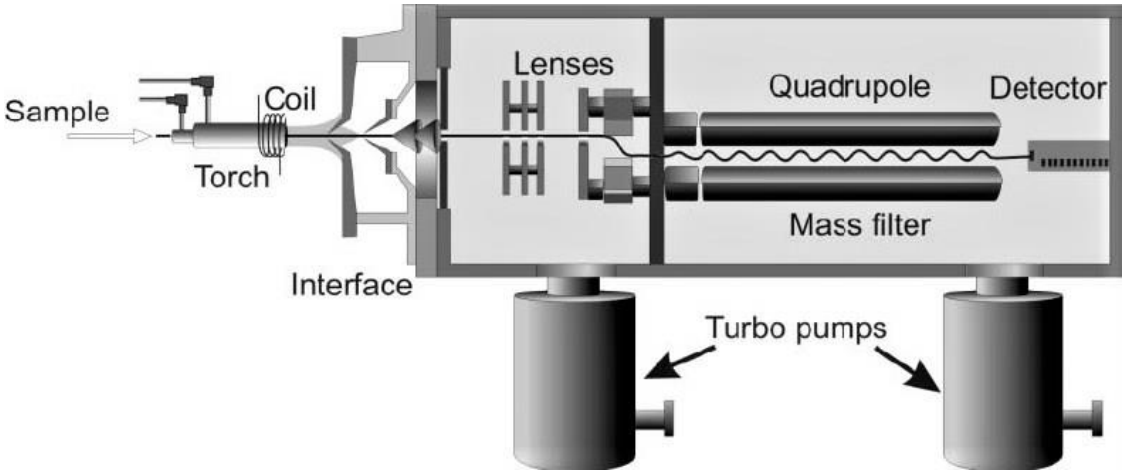
CHOP Method: Inductively coupled plasma/mass spectrometry (ICP/MS)

Image from PerkinElmer.com

- Analytical technique to measure elements at trace levels in biological fluids.

- Benefits: Low detection limits, multi-element measurements, low sample volume, high throughput, highly specific.

- Highly complex testing.



ICPMS, Clin Biochem Rev, 2019

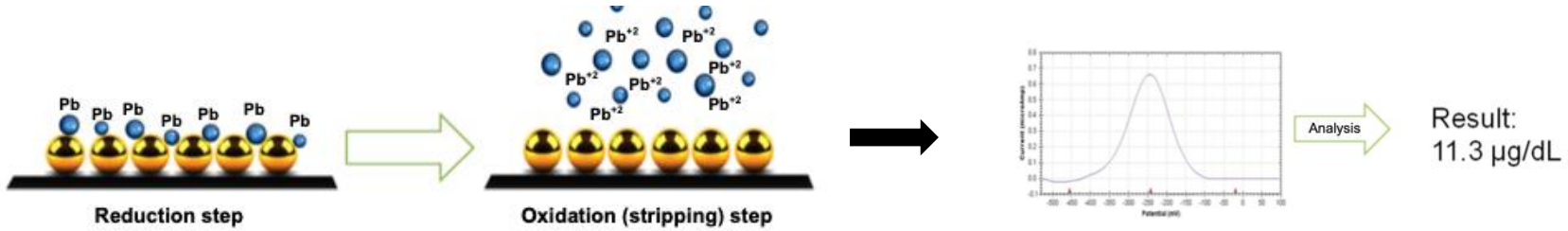
POCT Method: Magellan Diagnostics LeadCare

- LeadCare II
  - Flagship instrument
  - Only CLIA-waived blood lead analyzer
  - Works at the point-of-care
  - Fingerstick whole blood sample
  - 3 min to result
  - Measures down to 3.3 ug/dL
- LeadCare Ultra
- LeadCare Plus

Anodic Stripping Voltammetry (ASV)

Electrochemical technique used to determine ionic metal concentrations

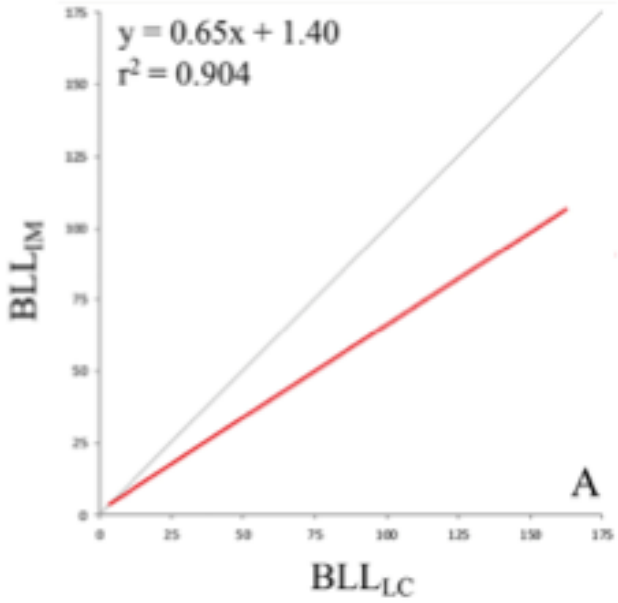
- Simple
- Rapid
- Low cost
- Relatively low sensitivity



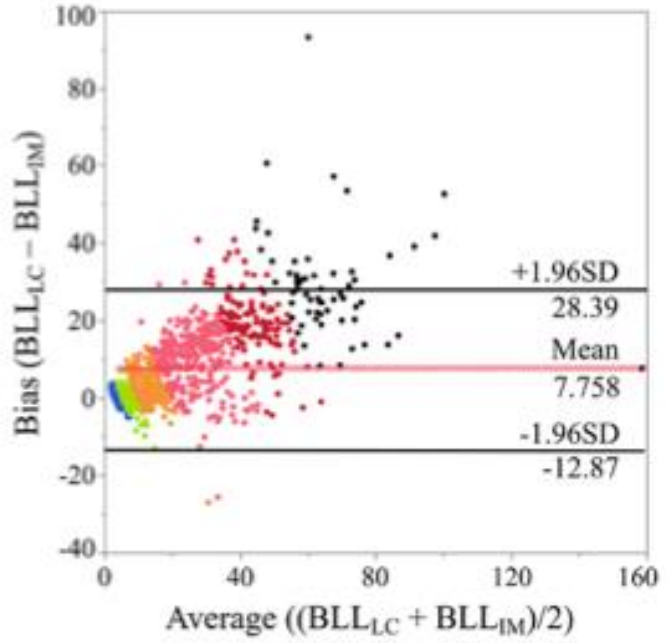
Analytical Performance: ICP/MS versus LeadCare II

- In general, BLLs correlate well between ICP/MS and LeadCareII.
- LeadCare II overestimates blood lead levels compared with ICP/MS.
- This bias is more significant at higher BLLs.

Regression Analysis



Bland-Altman Plot



LeadCare II is appropriate for screening purposes

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Nakata, et al. Chemosphere, 2021.

Analytical Performance: Blood Lead Proficiency Testing (PT) Programs

- CLIA-Approved Programs* (5 unknowns/3x per year)
  - College of American Pathologists (CAP)
  - Pennsylvania State Department of Health
  - Wisconsin State Laboratory of Hygiene (WSLH)
  - American Proficiency Institute (API)
- Non-Accredited Programs
  - CDC's Lead and Multielement Proficiency Program (LAMP)
- PT enrollment generally optional for waived testing (CAP and PA State are exceptions)

*Source: CMS.gov

CAP/AACC Blood Lead Survey (BL-B 2023)

Blood Lead - µg/dL or µmol/L	BL-06						BL-07						BL-08					
		µg/dL			µmol/L			µg/dL			µmol/L			µg/dL			µmol/L	
Method	N	MEAN	SD	CV%	MEAN	SD	N	MEAN	SD	CV%	MEAN	SD	N	MEAN	SD	CV%	MEAN	SD
Graphite furnace - Atomic Absorption Spectrophotometry	58	4.459	0.564	12.7	0.215	0.029	-	-	-	-	-	-	57	25.421	1.897	7.5	1.227	0.091
Inductively Coupled Plasma/Mass Spectrometry (ICP-MS)	88	4.376	0.271	6.2	0.211	0.013	33	0.415	0.087	21.0	0.020	0.004	89	24.718	1.248	5.1	1.193	0.060
Magellan LeadCare II (waived)	33	6.533	0.936	14.3	0.316	0.046	-	-	-	-	-	-	32	29.372	2.045	7.0	1.418	0.099

Blood Lead - µg/dL or µmol/L	BL-09						BL-10					
		µg/dL			µmol/L			µg/dL			µmol/L	
Method	N	MEAN	SD	CV%	MEAN	SD	N	MEAN	SD	CV%	MEAN	SD
Graphite furnace - Atomic Absorption Spectrophotometry	57	11.382	1.075	9.4	0.549	0.052	58	50.360	4.071	8.1	2.431	0.196
Inductively Coupled Plasma/Mass Spectrometry (ICP-MS)	89	11.018	0.622	5.6	0.532	0.030	88	49.824	2.634	5.3	2.405	0.127
Magellan LeadCare II (waived)	32	14.116	1.365	9.7	0.681	0.065	28	56.932	4.774	8.4	2.748	0.231

Evaluation Criteria:
± 10% or 4 µg/dL (whichever is greater)

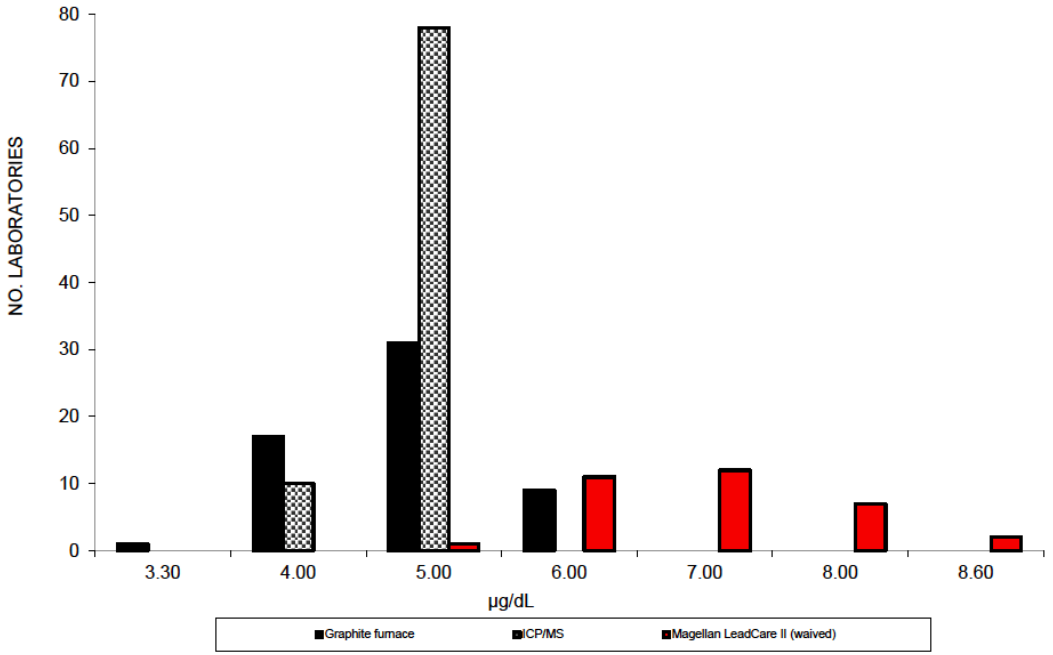
CAP/AACC Blood Lead Survey (BL-B 2023)

BL-06

Graphite furnace: N=58
MEAN=4.459 SD=0.564 CV=12.7

ICP/MS: N=88
MEAN=4.376 SD=0.271 CV=6.2

Magellan LeadCare II (waived): N=33
MEAN=6.533 SD=0.936 CV=14.3

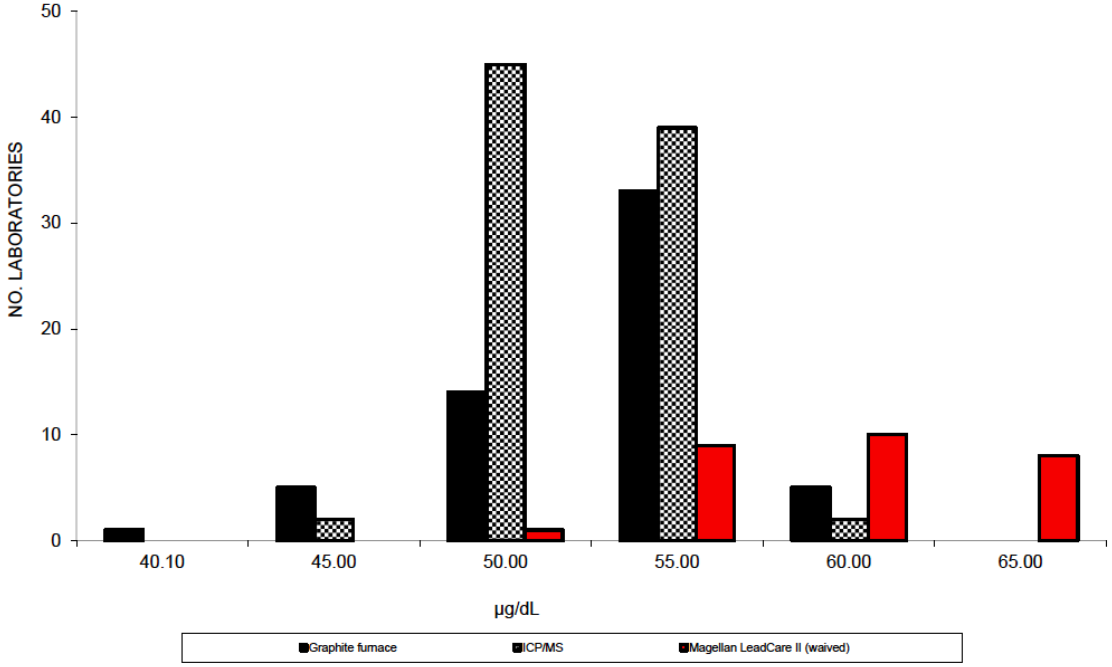


BL-10

Graphite furnace: N=58
MEAN=50.360 SD=4.071 CV=8.1

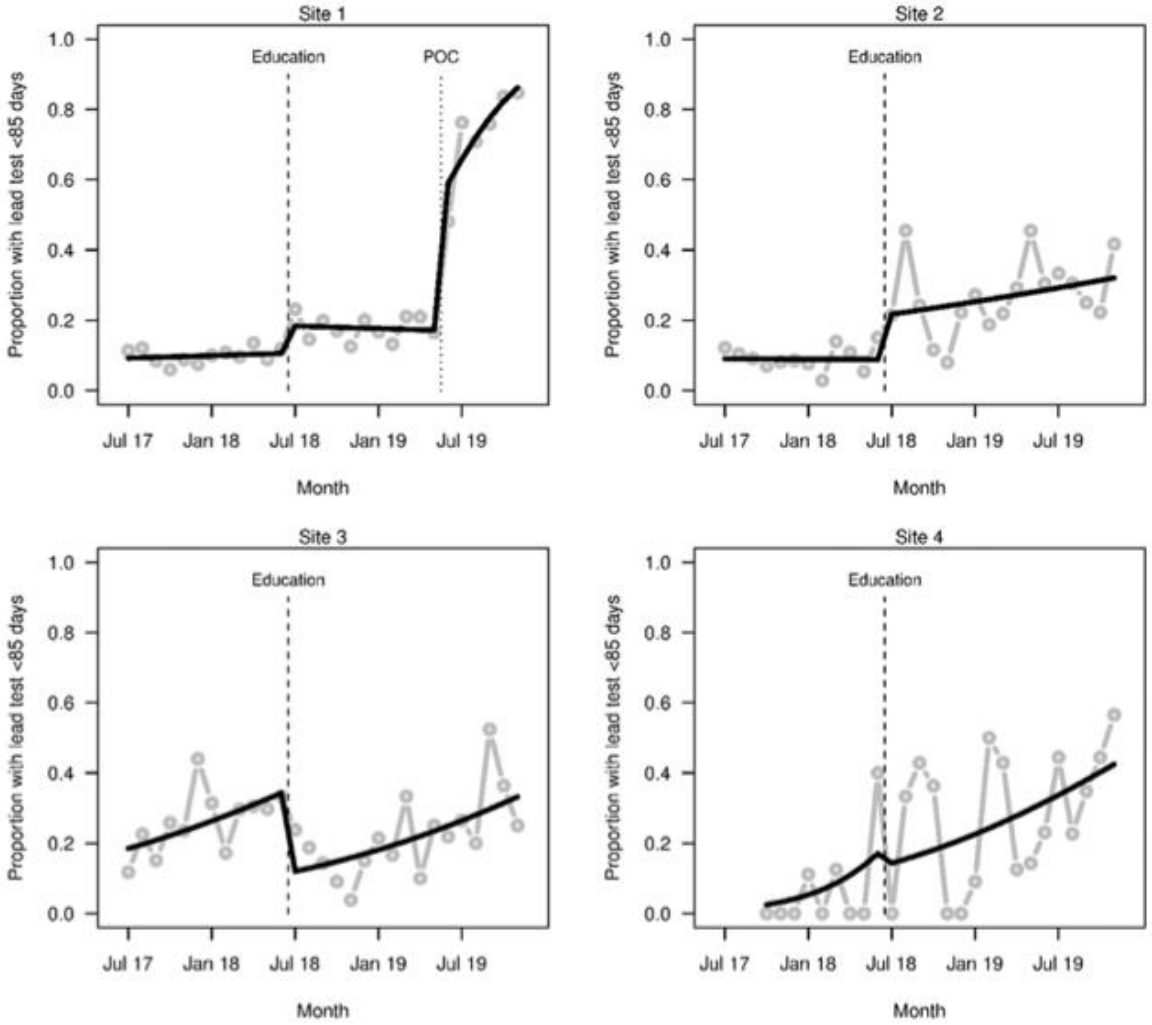
ICP/MS: N=88
MEAN=49.824 SD=2.634 CV=5.3

Magellan LeadCare II (waived): N=28
MEAN=56.932 SD=4.774 CV=8.4



LeadCare overestimates blood lead levels compared with gold standard methods

POCT Improves Lead Screening Rates



- Study carried out in 4 pediatric primary care practices in a south central PA academic health system.
- 2 main interventions: provider education (all sites) and implementation of POC testing (1 site).
- POCT is more convenient for providers and families and less invasive for patients.

Carnahan et al. The Journal of Pediatrics, 2021.

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Analytical Considerations: Summary

ICP/MS or AAS	LeadCare
Performed in clinical lab: patient may not go to phlebotomy/ref lab	Performed at the point-of-care: within flow of patient care
Multi Day TAT: provider needs to follow up, patient may need to return to office for follow up/next steps	Results within minutes: patient/family follow up and education in real time
Highly complex testing: requires highly trained staff and regulatory oversight	Potentially waived: few regulatory requirements
Confirmatory BLL: diagnostic if performed via venous sample	Screening BLL: may need to return for confirmation if elevated
Highly accurate and precise: appropriate for diagnostic testing and measuring treatment response	Accurate and precise: appropriate for screening but not diagnostic testing, can have interference by other metals
Very low limits of detection (<1 ug/dL): can accommodate a lower BLRV	Limited at the lower end of detection: cannot accommodate a lower BLRV

Post-analytical Considerations: Reporting and Management of Elevated Blood Lead Levels

- Patient Report Considerations:
  - Elevated capillary samples should be confirmed with a venous specimen collected in metal-free tube (tan K2EDTA).
  - Elevated results from non-certified lead-free tubes may be due to contamination.
  - Lab-Developed Test Comment if performed by ICP/MS or AAS.

Post analytical Considerations: Reporting and Management of Elevated Blood Lead Levels

Table 1: Summary of Blood Lead Tests Performed in 2021 by Age Category

Age category*	Total number of tests†	Capillary test#		Venous test	
		N	%	N	%
0–23 months (under 2 years)	94,597	64,040	67.70	30,557	32.30
0–71 months (under 6 years)	168,687	108,006	64.03	60,681	35.97
0–15 years	175,484	108,946	62.08	66,538	37.92

Table 3: Elevated Blood Lead Confirmation Status per 2016 CDC Case Definition* by Age Category, 2021

	Children aged 0–23 months		Children aged 0–71 months	
	N	% of total	N	% of total
Total number of children tested	88,311	100.00	156,018	100
Confirmation status				
Not elevated (< 5 µg/dL)**	85,440	96.75	149,208	95.64
Unconfirmed elevated (≥ 5 µg/dL)†	850	0.96	1,960	1.26
Confirmed 5–9.9 µg/dL	1,414	1.60	3,353	2.15
Confirmed ≥ 10 µg/dL	607	0.69	1,497	0.96

2021 Childhood Lead Surveillance Report, PA DOH

Post analytical Considerations: Reporting and Management of Elevated Blood Lead Levels

Medical Management Recommendations for Confirmed Blood Lead Levels	
Confirmed BLL	**Recommended Actions Based on Confirmed BLL**
< 3.5 µg/dL	• Anticipatory guidance about common sources of lead exposure and how to prevent exposure. • Routine assessment of developmental milestones and nutritional status with a focus on iron and calcium intake. • Repeat blood lead level in 6-12 months if the child is at high risk or risk changes during the timeframe.
3.5 – 19 µg/dL	• Re-test BLL at recommended intervals to ensure BLL is not rising and lead exposures are controlled. • Take environmental history to identify potential sources of exposure. Provide education on exposure prevention. • Consider testing young siblings and other children in the home who may be exposed. • Ensure iron sufficiency with testing and treatment. Consider multivitamin with iron. • Provide nutritional counseling related to calcium and iron. Encourage consumption of fruit and iron-enriched foods. Refer to supportive services as needed (e.g. WIC). • Perform structured developmental screening and monitoring, as lead's impact on development may manifest over years. Refer to early intervention for evaluation if developmental delays suspected or diagnosed. • Refer to state or local health department for environmental investigation if confirmed BLL is ≥10 µg/dL or as indicated by local health department.
20 – 44 µg/dL	**Follow recommendations for BLL 3.5-19 µg/dL as listed above.** • Complete history and physical exam assessing for signs and symptoms related to lead. • Consider abdominal x-ray based on history (e.g. history of pica or excessive mouthing behaviors). • Contact state or local health department or for guidance.
≥ 45 µg/dL	**URGENT: Follow guidance above, plus:** • Complete history and physical exam including detailed neurological exam. • Obtain abdominal X-ray and initiate bowel decontamination if indicated. • Consider chelation therapy and/or hospitalization. Child should be discharged to a lead-safe environment. • Consult with an expert about chelation therapy. Contact Pediatric Environmental Health Specialty Unit (1-800-421-9916) or Poison Control Center (1-800-222-1222).

Source: Adapted from: CDC, Recommended Actions Based on Blood Lead Levels: https://www.cdc.gov/nceh/lead/advisory/acclpp/actions-blls.htm and Pediatric Environmental Health Specialty Unit: https://www.pehsu.net/Lead_Exposure.html

Source: Nebraska Department of Health and Human Services, 4/4/22

Post analytical Considerations: Reporting and Management of Elevated Blood Lead Levels

Table 2: Schedule for Follow-Up Blood Lead Testing[a]

Venous blood lead levels (µg/dL)	Early follow up testing (2–4 tests after initial test above specific venous BLLs)	Later follow up testing after BLL declining
≥3.5–9	3 months*	6–9 months
10–19	1–3 months*	3–6 months
20–44	2 weeks–1 month	1–3 months
≥45	As soon as possible	As soon as possible

CDC.gov

Summary

- There is no safe level of lead exposure for children – children are most at risk of lead poisoning due to their rapid development.
- Primary prevention is the most reliable and cost-effective measure to protect children from lead exposure.
- Laboratory and POCT methods are acceptable for lead screening.
- Elevated screening blood lead levels need to be confirmed with a venous sample by a gold standard method.

Questions?

e-mail: polskyt@chop.edu

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