

# Commentary on Potential Risk From Thimerosal for Infants

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# Key Points

- What is the maximum safe dose of thimerosal that can be administered on one day?
- Is ethylmercury from thimerosal additive to methylmercury?
- **Not:** Vaccinating vs not vaccinating. It is making vaccines as safe as possible.

# FDA Risk Assessment

- Initial reaction to FDA assessment:
  - surprise, disbelief
- Calculations correct
- Why missed?
  - Label: thimerosal concentration (.01%)
  - Guidelines for exposure to Hg in ug

# Thimerosal is Neurotoxic in Large Doses

- HBIG and IVIG
  - Lowell. Lancet 1996;347:380
  - Matheson. J Pediatr 1980;97:153
- IM Chloramphenicol
  - Axton. Postgrad Med J 1972;48:417
- Painting omphaloceles
  - Fagan. Arch Dis Child 1977;52:962
- Irrigation of ears
  - Rohyans. J Pediatr 1984;104:311
- What is safe for the developing brain?

# FDA Risk Assessment

## Maximum Cumulative Exposure

- Routine schedule:
  - Birth, 2, 4, 6 months
  - 187.5 ug maximum
  - Exceeded EPA RfD for most children
  - Exceeded ATSDR for < 5<sup>th</sup> percentile

# FDA Risk Assessment

## Maximum Cumulative Exposure

- Accelerated immunization schedule:
  - Birth, 6, 10, 14 weeks
  - Pertussis outbreaks, travel to developing countries
  - Exceeded ATSDR guidelines for many children

# What Time Period Should be Used for Cumulating Exposures?

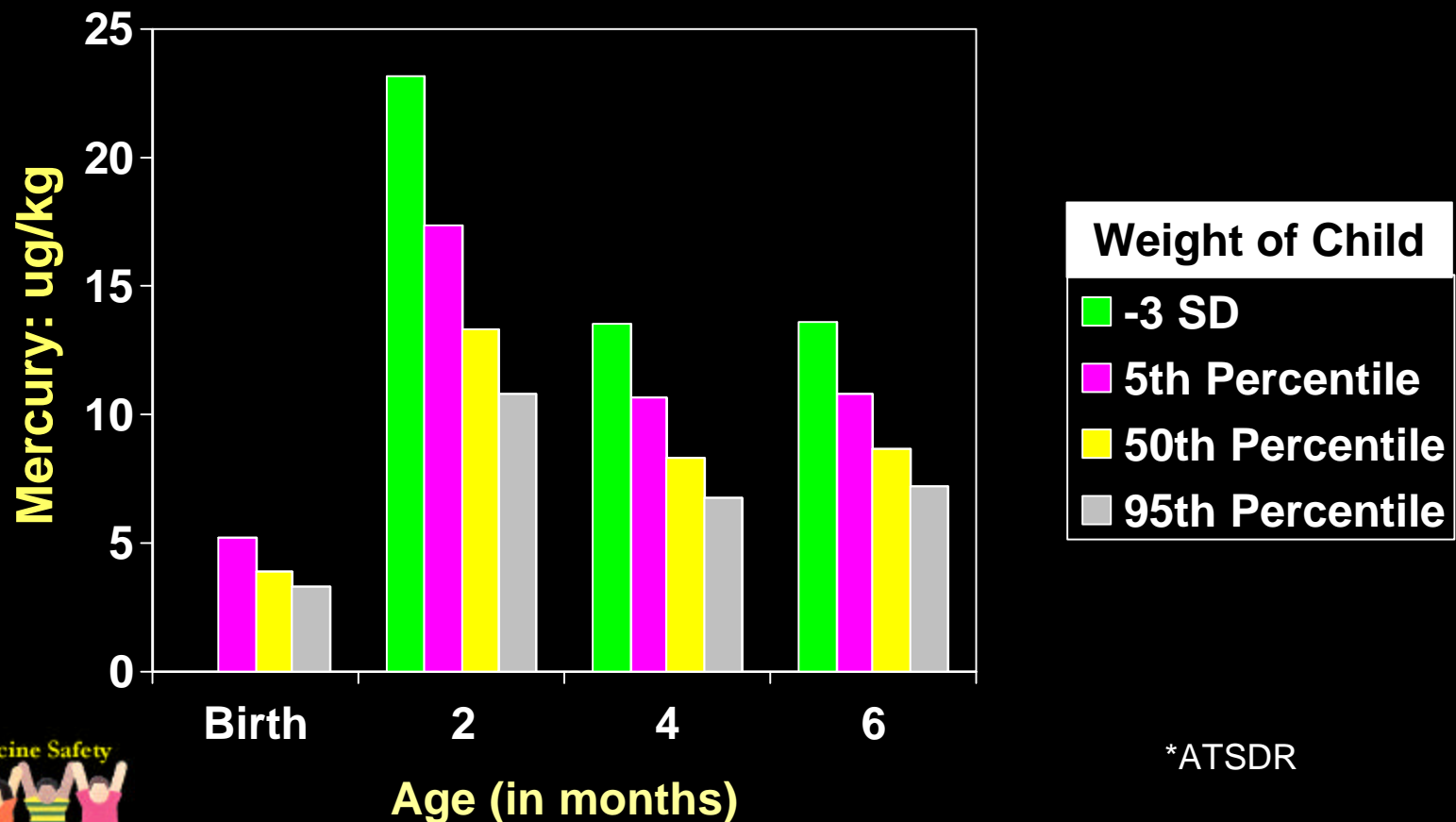
- Birth to 6 months? 187.5 ug
- Birth to 3 months-accelerated schedule? 175 ug?
- Birth to 2 months? 75 ug
- One day? 62.5 ug

# Weight in Kg for **Girls** by Percentile and Age

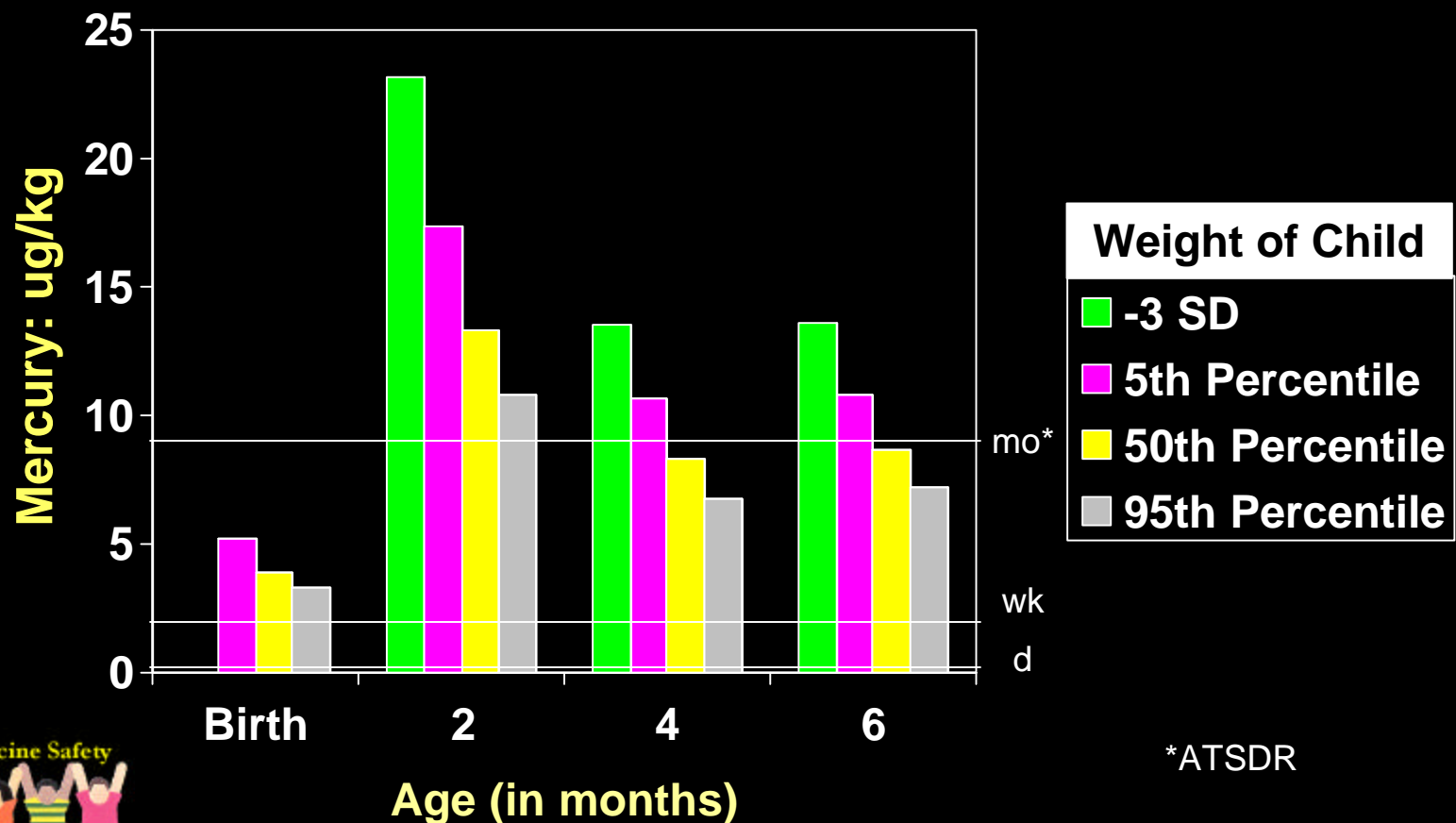
Age	Percentile			
	-3 SD	5th	50th	95th
Birth	1.8	2.4	3.2	3.8
2 mo	2.7	3.6	4.7	5.8
4 mo	3.7	4.7	6	7.4
6 mo	4.6	5.8	7.2	8.7



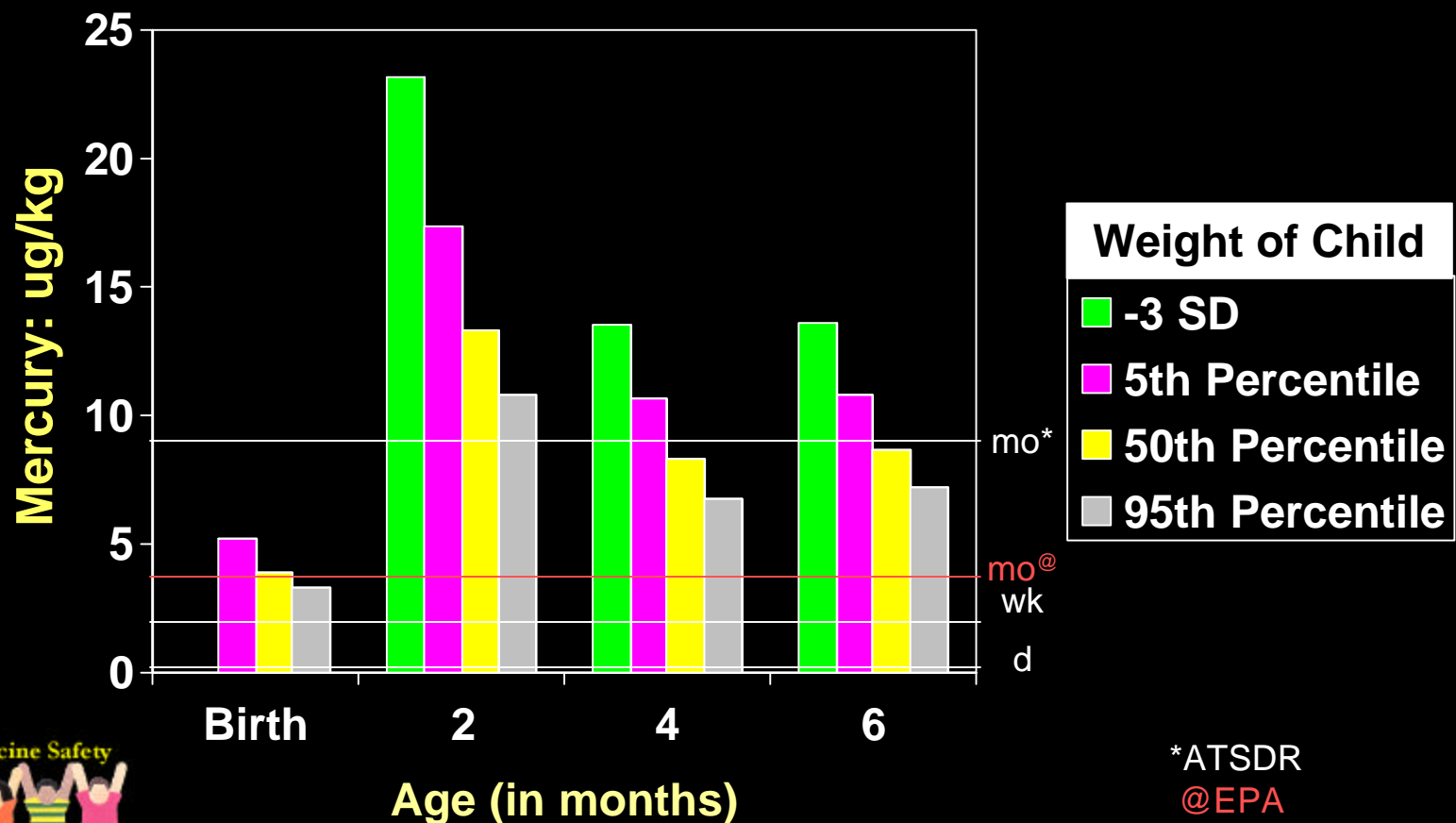
# Mercury (ug/Kg) Administered by Age and Weight If Thimerosal-containing Vaccines Are Given for Hepatitis B, Hib, and DTaP



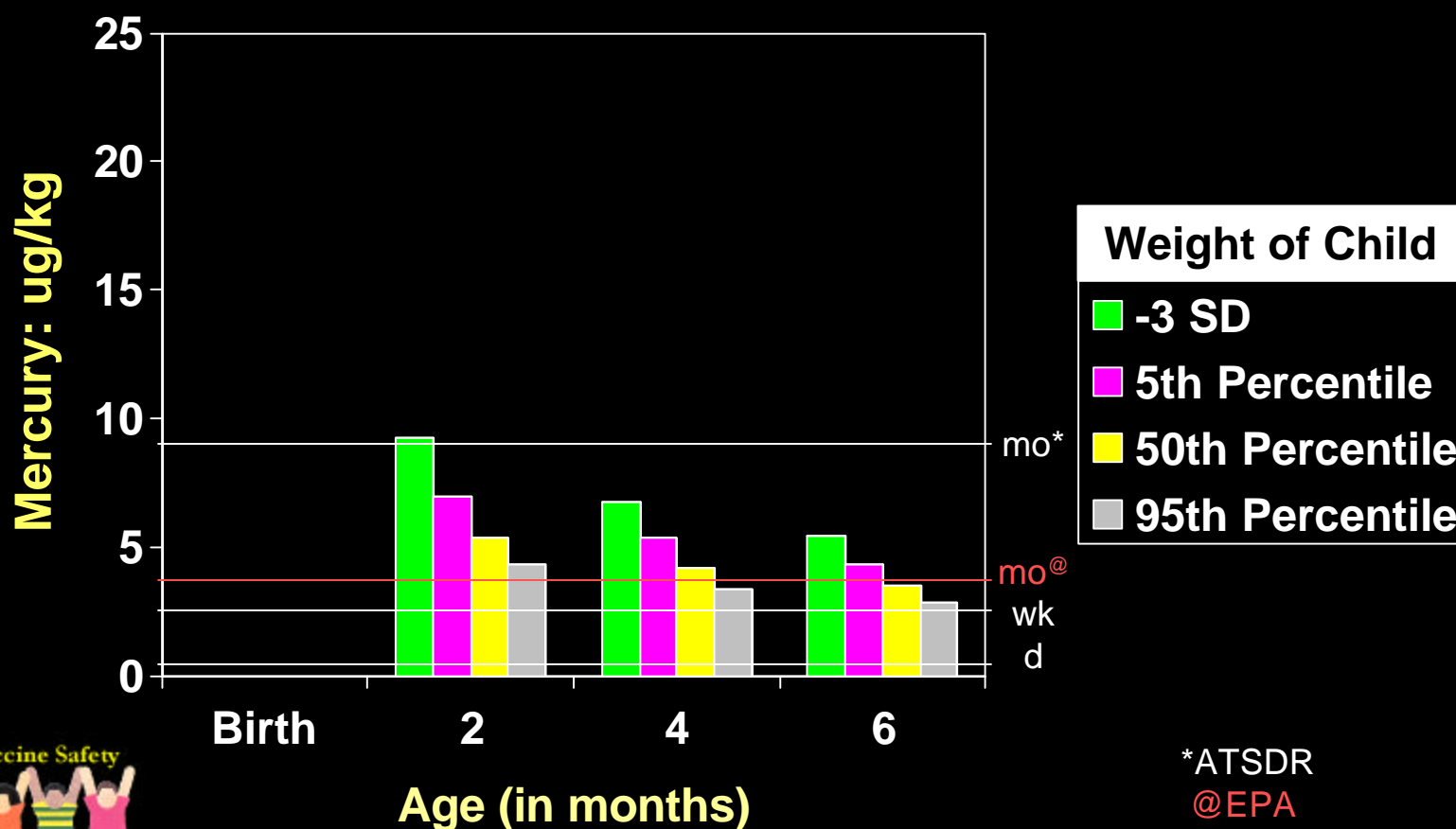
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# Mercury (ug/Kg) Administered by Age and Weight If Thimerosal-containing Vaccines Are Given for Hepatitis B, Hib, and DTaP



# Amount of Mercury Administered If Only One Thimerosal-containing Vaccine Is Given (Hib or DTaP)



# Summary of MeHg Reference Values

AGENCY	Values (ug/kg/day)	TERMINOLOGY
EPA	0.1	RfD
FDA	0.4	ADI
ATSDR	0.3	MRL
WHO	3.3 ug/kg/wk	PTWI



# Toxicological Effects of Methylmercury

NATIONAL RESEARCH COUNCIL

Committee on  
the  
Toxicological  
Effects of  
Methylmercury

Board on  
Environmental  
Studies and  
Toxicology

Commission on  
Life Sciences

National  
Research  
Council

Washington DC  
National  
Academy Press  
2000

Institute for Vaccine Safety



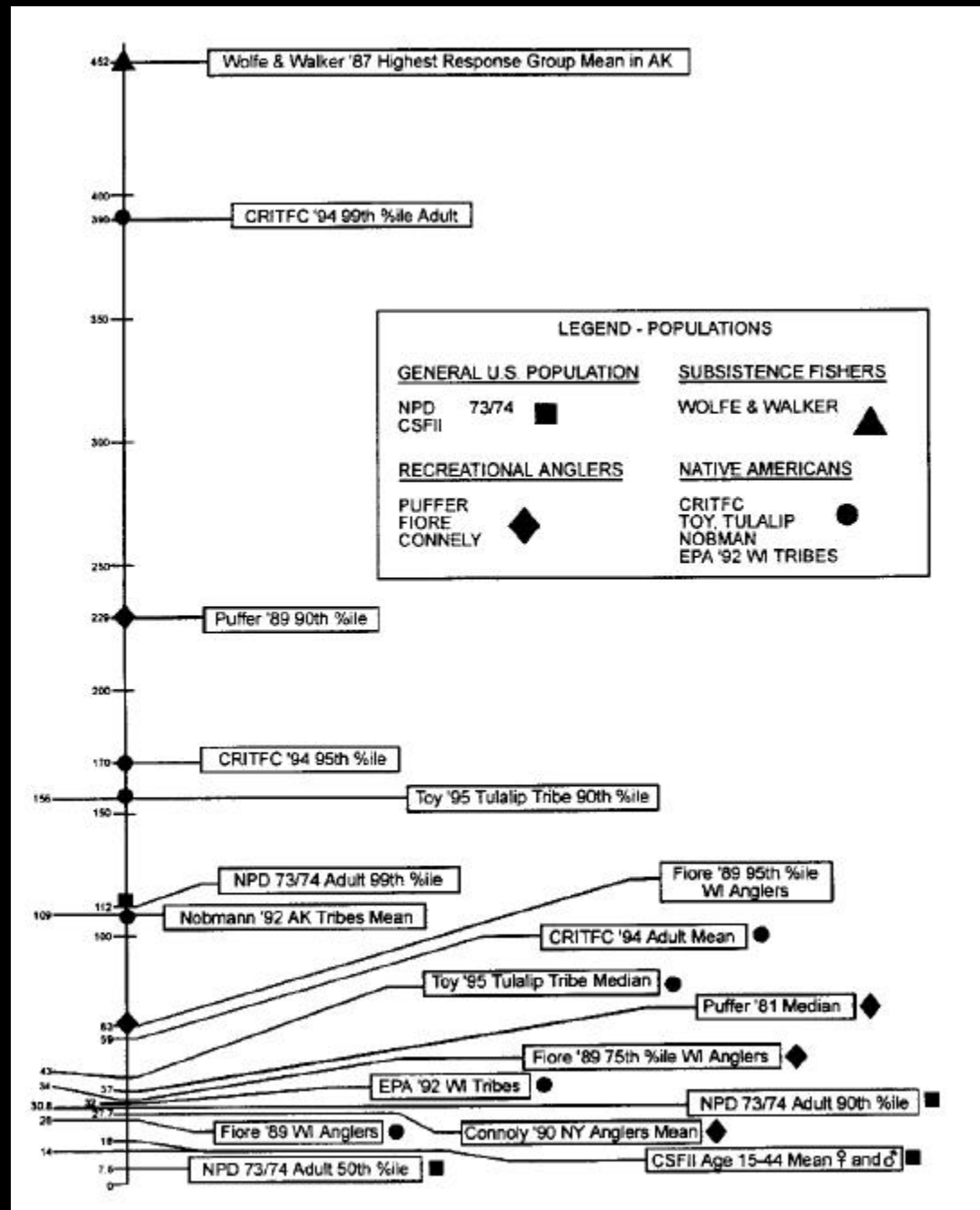
Johns Hopkins University

# National Research Council Review of Methylmercury

- RfD should be 0.1 ug/Kg/d
- Over 60,000 children born per year at risk for neurodevelopmental effects
- Other forms of mercury should be taken into consideration

# Fish Consumption Rates of Various Populations

Source: EPA Mercury Study Report to Congress Volume 1: Executive Summary EPA-452/R-97-003, Dec 1997





# **PROTECT YOUR KIDS RELEASE YOUR CATCH**

**Due to MERCURY CONTAMINATION of Inland Waters;  
DO NOT EAT WARM WATER FISH SPECIES:**

**If You Are Pregnant, Nursing, May Soon Become Pregnant or Are Less  
Than 8 Years Old**

**Additionally, Consumption of Cold Water Species Should Be Limited to 1 Meal Per  
Month. Other Individuals Limit Consumption of Warm Water Species to 2-3 Meals Per**



**While providing certain health benefits, eating fish caught from these waters may also expose you to chemicals which can cause cancer, birth defects, and learning disabilities. Animals like the bald eagle, loon, and otter are also at risk. Scientists have documented deformities, reproductive problems, and tumors in fish, amphibians, mammals, birds, and other wildlife in polluted water bodies.**

**This posting is a public service of the **Maine Toxins Action Coalition [MTAC]****

**For a full copy of the State consumption advisories and more information on toxins in the environment call MTAC at 1-800-287-2345 or Maine Bureau of Health at 287-6455**

**Maine fish consumption advisories are not restricted to mercury contamination.**

**Non-posted waters should NOT be assumed to be free of contaminants.**

# Estimates of Methylmercury Levels in Women of Childbearing Age in the United States

- EPA dietary consumption
  - 7% >.1 ug/Kg/d, 1% >.37ug/Kg/d
- NRC modeling
  - 60,000 children born per year to mothers with elevated levels
- CDC NHANES\* blood mercury
  - Mean 1.2 ppb (90<sup>th</sup> % 6.2 ppb)
  - 10% have levels within 1/10<sup>th</sup> of potentially hazardous levels

# FDA Fish Advisory

## March 2001

- Pregnant women and women of childbearing age should avoid:
  - Shark, mackerel, swordfish, tilefish
- Swordfish ~1 ppm methylmercury
  - 28.5 ug Hg per ounce

# July 1999

- AAP/PHS joint statement
  - Could exceed guidelines for MeHg
  - Delay hep B vaccine for infants born to HBsAg negative women
  - Reduce or eliminate thimerosal
- AAP interim report
  - Amounts of Hg in each vaccine
  - Limit exposure to Hg from other sources

# Suggested Guidelines (1999) for Limiting Infant Exposure to Thimerosal in Vaccines

- Preference for vaccines without thimerosal preservative
- No more than one vaccine with thimerosal preservative per regularly scheduled visit

# DTaP, Hep B, and Hib Vaccines Without Thimerosal Preservative July 1999

## DTaP

- Infanrix

## Hepatitis B

- COMVAX

## Hib

- ActHIB
- Omni Hib
- HibTITER  
Single dose
- PedvaxHIB  
Liquid
- COMVAX

# DTaP, Hep B, and Hib Vaccines Without Thimerosal Preservative July 2001

## DTaP

- Infanrix
- Tripedia

## Hepatitis B

- COMVAX
- Recombivax HB  
“preservative free”
- Engerix B  
“preservative free”

## Hib

- ActHIB
- Omni Hib
- HibTITER  
Single dose
- PedvaxHIB  
Liquid
- COMVAX

# **AMERICAN ACADEMY OF PEDIATRICS**

Lynn R. Goldman, MD, MPH; Michael W. Shannon, MD, MPH; and the  
Committee on Environmental Health

## **Technical Report: Mercury in the Environment: Implications for Pediatrics**



**Pediatrics 2001;108(1):197**



# VSD Studies

- Delayed speech, language, LD
  - Multifactorial etiologies
  - Large studies needed
- Harvard Pilgrim study:
  - Power?
- Data inconclusive, but suggestive of an effect from thimerosal

# Why Additional Studies Are Needed

- The public deserves an answer:
  - If toxicity, VICP?
- Exposures continuing in other countries
  - Obligation to find answers
  - Assistance will be needed for removal if toxic effects demonstrated

# Additional Studies Needed

- CDC/NIH cohort follow-up study
  - Strongest design
  - Power uncertain for some outcomes
  - Power likely to be greater for more subtle effects
- Other populations with high baseline methylmercury exposures
  - Case-control studies?

# Animal Studies Needed

- Is ethylmercury **equivalent** to methylmercury?
- Is ethylmercury **additive** to methylmercury?
- Are **bolus doses** more toxic than small daily doses?

# Lessons from Thimerosal

- FDA, manufacturers, and advisory bodies can mobilize and act rapidly when indicated to improve safety.
- Actions taken have minimized potential risks to children from mercury
- Public needs to be confident that vaccines are made as safe as possible

# Encourage IOM to Stop Using: “The Evidence is Inadequate to Accept or Reject a Causal Relation”

- Not informative
- Overused -always some doubt
- Misinterpreted as there is scientific evidence supporting hypotheses
  - Hepatitis B and MS
  - MMR and autism
- Just summarize the evidence