



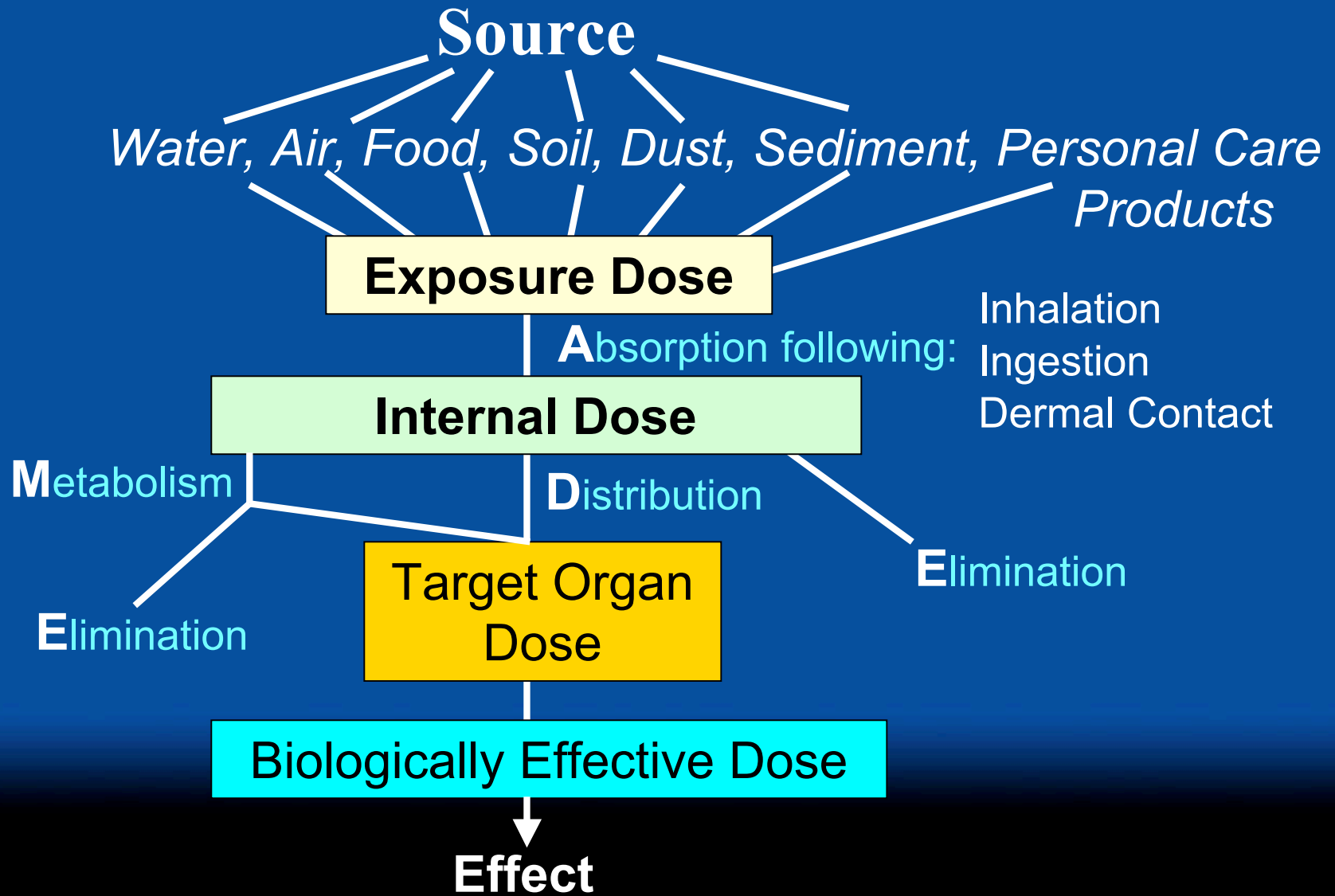
Biomonitoring in NHANES

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Exposure Pathway



Biomonitoring

Assessment of internal dose by measuring the parent chemical (or its metabolite or reaction product) in human blood, urine, milk, saliva, adipose, or other tissue.

CDC's *Second National Report on Human Exposure* – data from NHANES 1999-2000

Urine

Metals (13)

PAH metabolites

Phthalate metabolites

Pesticides

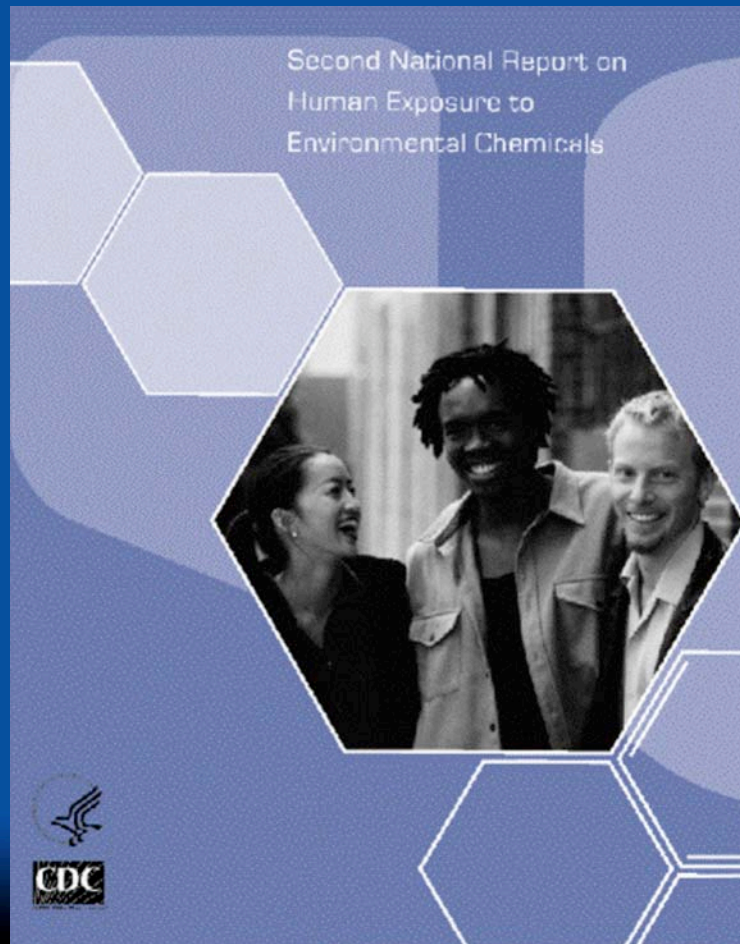
Organophosphorus

Carbamates

Herbicides

Repellants

Phytoestrogens



Blood

Lead

Cadmium

Mercury

Serum

Dioxins

Furans

PCBs

Organochlorine pesticides

Cotinine

Released: March 2003

www.cdc.gov/exposurereport

National Report on Human Exposure to Environmental Chemicals

What it is:

An ongoing (every 2 years) biomonitoring assessment of the exposure of the U.S. population to selected environmental chemicals

Matrices monitored: Urine; blood and its components

Major Findings: U.S. Population-based Reference Ranges

- Geometric means
- 10th, 25th, 50th, 75th, 90th, and 95th percentiles
- Age, sex, race/ethnicity breakout

National Health and Nutrition Examination Survey

- Conducted by the National Center for Health Statistics/CDC
- Population is a stratified, complex, multistage probability sample of the civilian, noninstitutionalized U.S. population
- Estimates are probability based for the U.S. population
- Includes detailed history, physical, and laboratory exam
- Primary focus is generation of clinical data, but exposure data can be linked to clinical data and nutritional status

NHANES 1999-2000

- About 5000 participants annually from 15 locations
- Continuous annual survey
- Includes home interview
- Oversampled African Americans, Mexican Americans, adolescents (12-19 years), older Americans (≥ 60 years); pregnant women. In 2000 also low income whites
- More information:
<http://www.cdc.gov/nchs/nhanes.htm>

Goals of *National Report*

In American population and subpopulations (age, sex, race/ethnicity)

- Assess exposure to various chemicals (which?)
- Establish national “reference ranges” of these chemicals (blood, urine)
- Track, over time, trends in these “reference ranges”
- Help set priorities on linking exposure to health outcomes

Public Health Uses of *National Report*



- Assess effectiveness of efforts to reduce exposures (lead in gasoline; FQPA; POPs) in all Americans
- In some cases, provide data for establishing source (pattern recognition, e.g., gasoline, dioxins/furans)
- Provide data for risk assessment (dose-response and exposure assessment)
- Provide data for linking environmental exposure data with interactions with genes, nutrition, and demographic data to eventually link with health outcome data

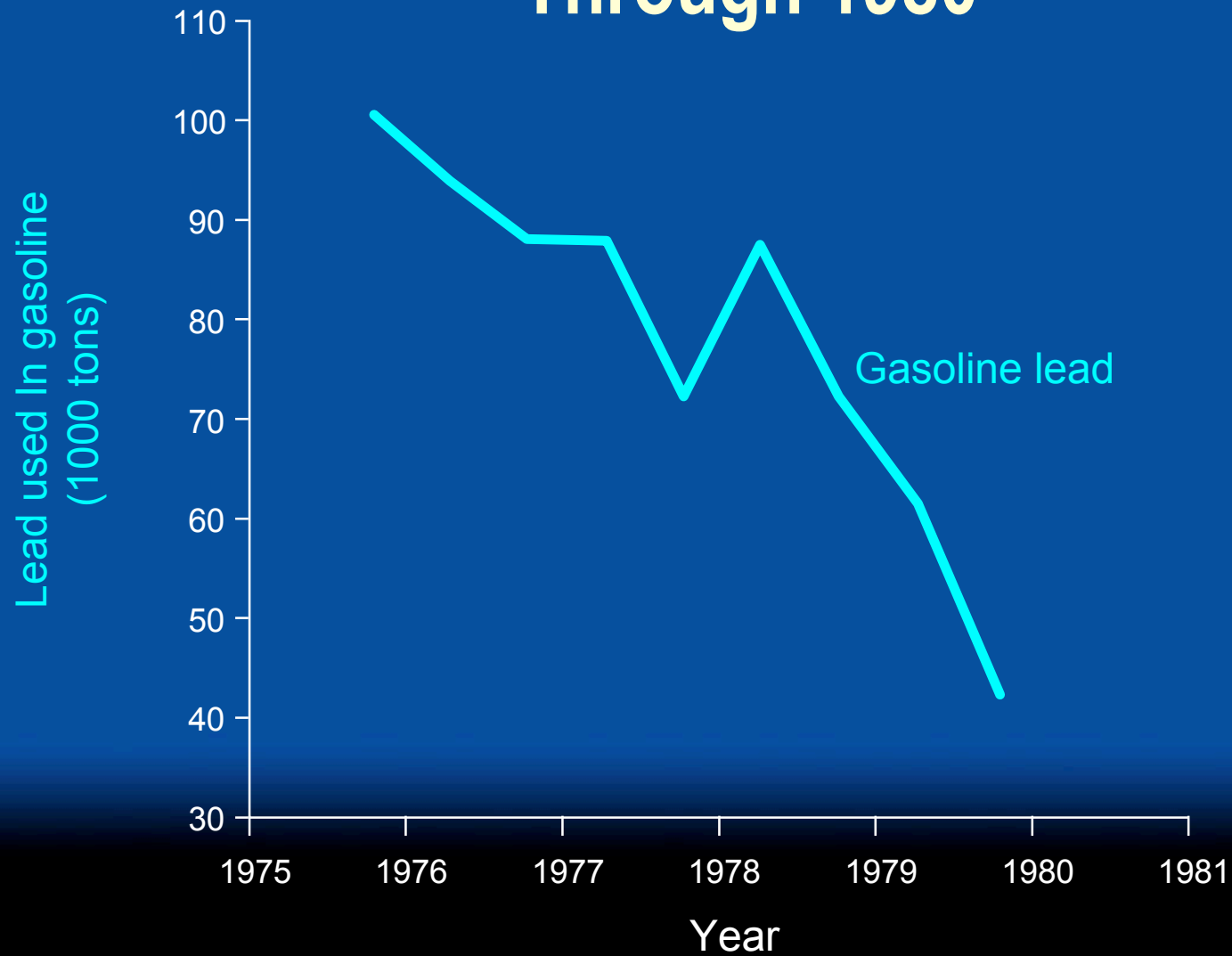
Interpreting Data in the *Report*

- The presence of a chemical in the body does not mean it causes disease
- For many chemicals in the *Report*, more research is needed to interpret these levels
- The *Report* provides new exposure data, but does not identify levels that cause disease
 - ◆ Additional studies are needed

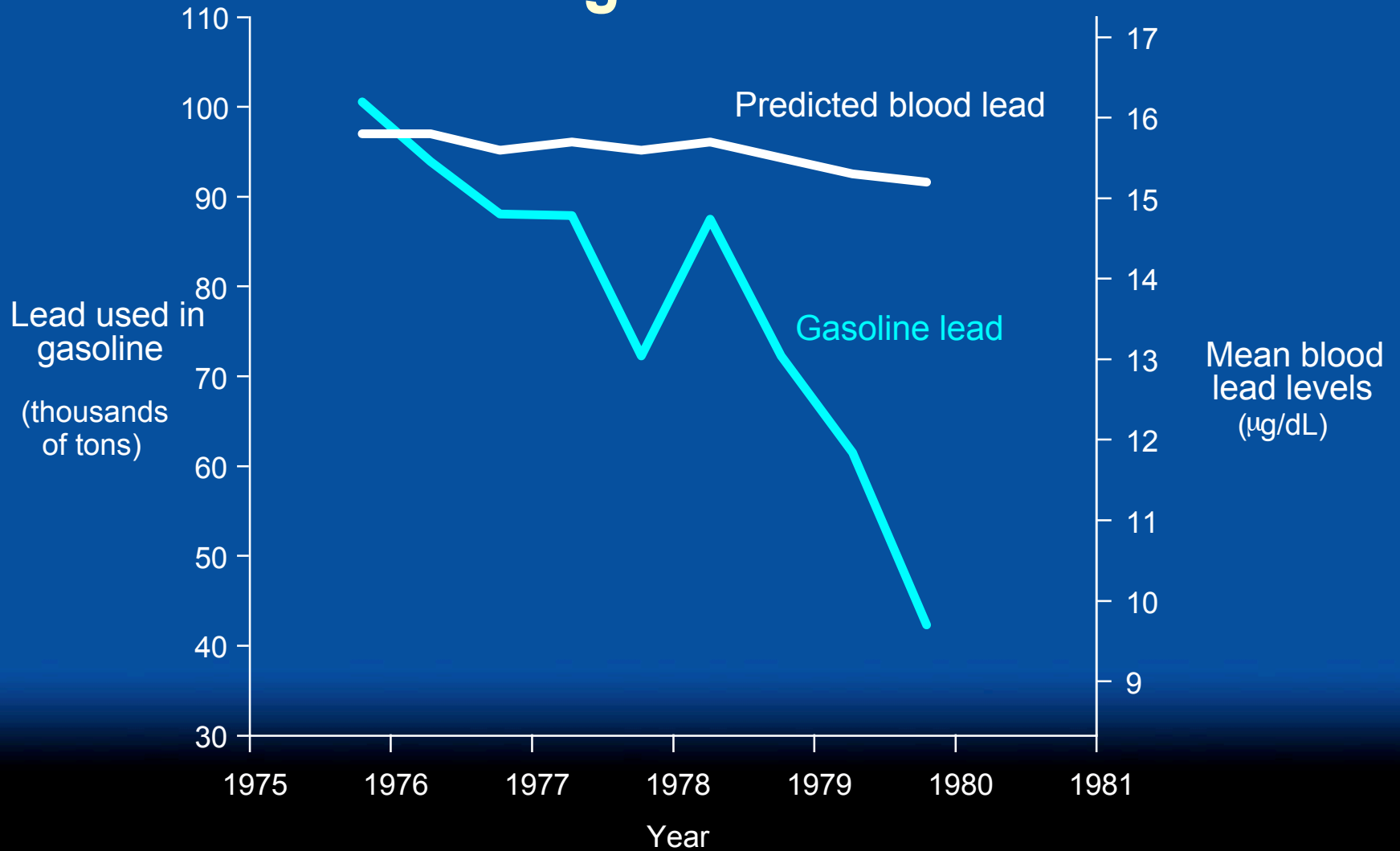
Lead

Blood lead levels (BLLs)
1 year of age and greater

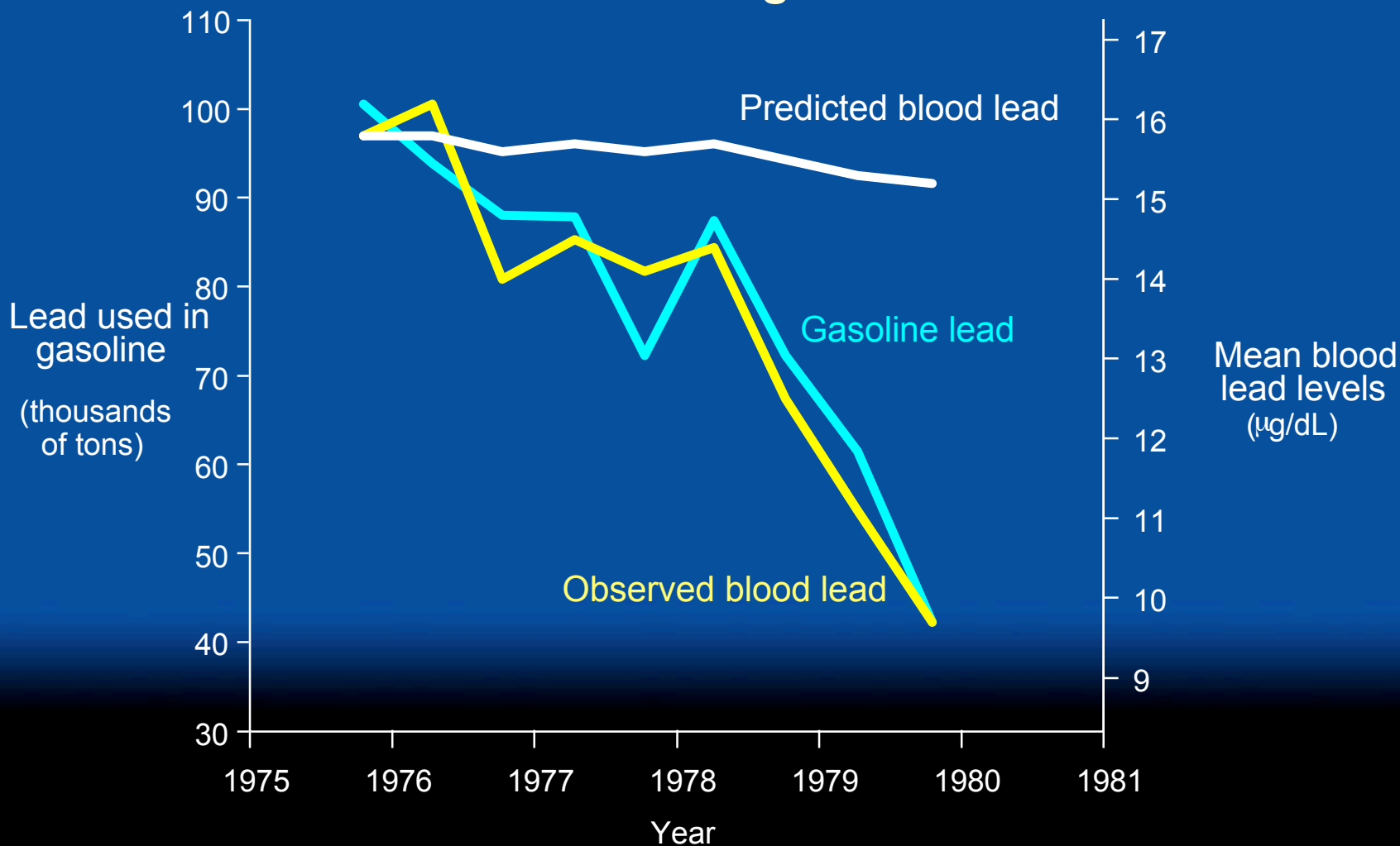
Lead Used in Gasoline Declined from 1976 Through 1980



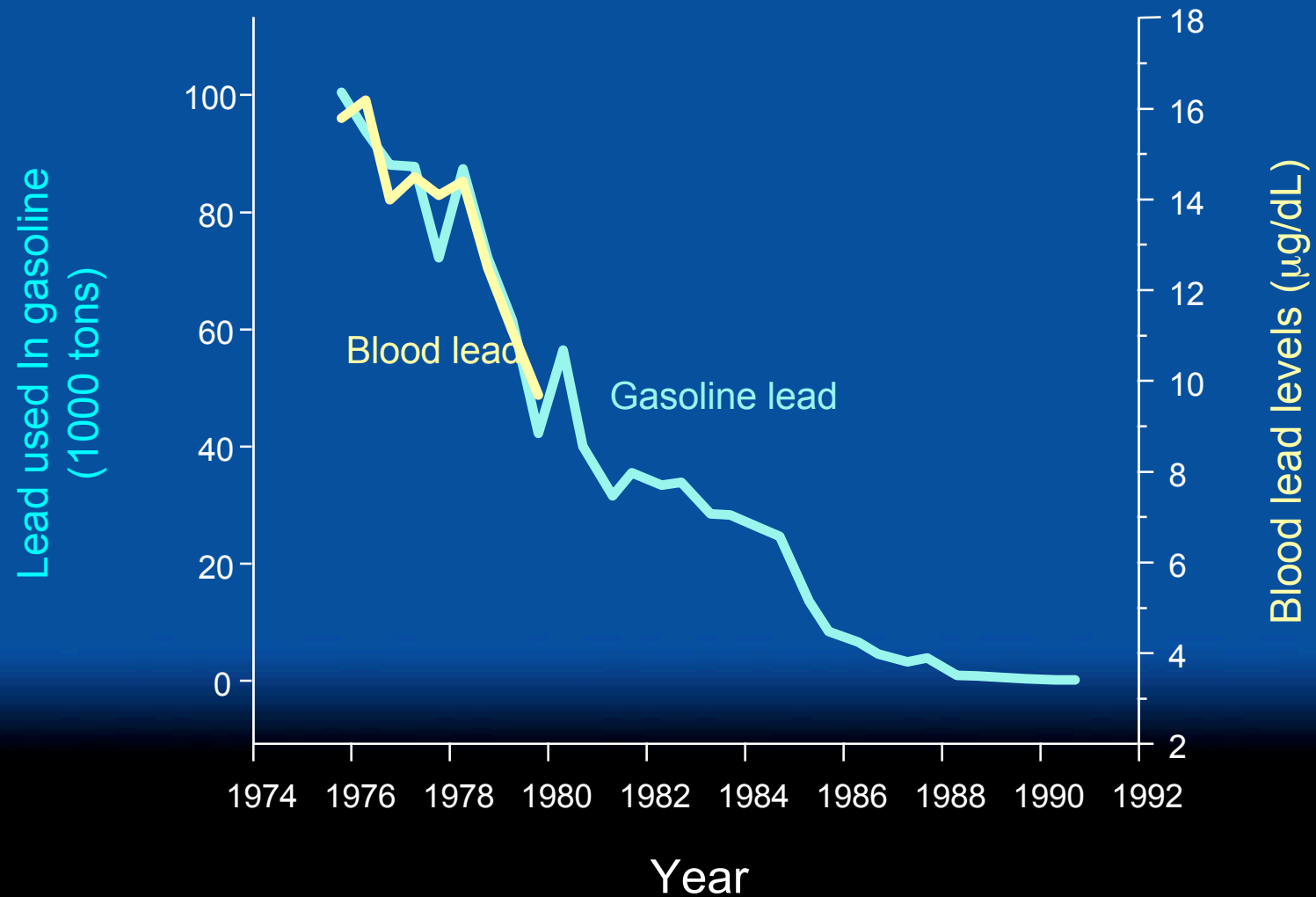
Predicted Blood Lead Changes with Decreasing Gasoline Lead



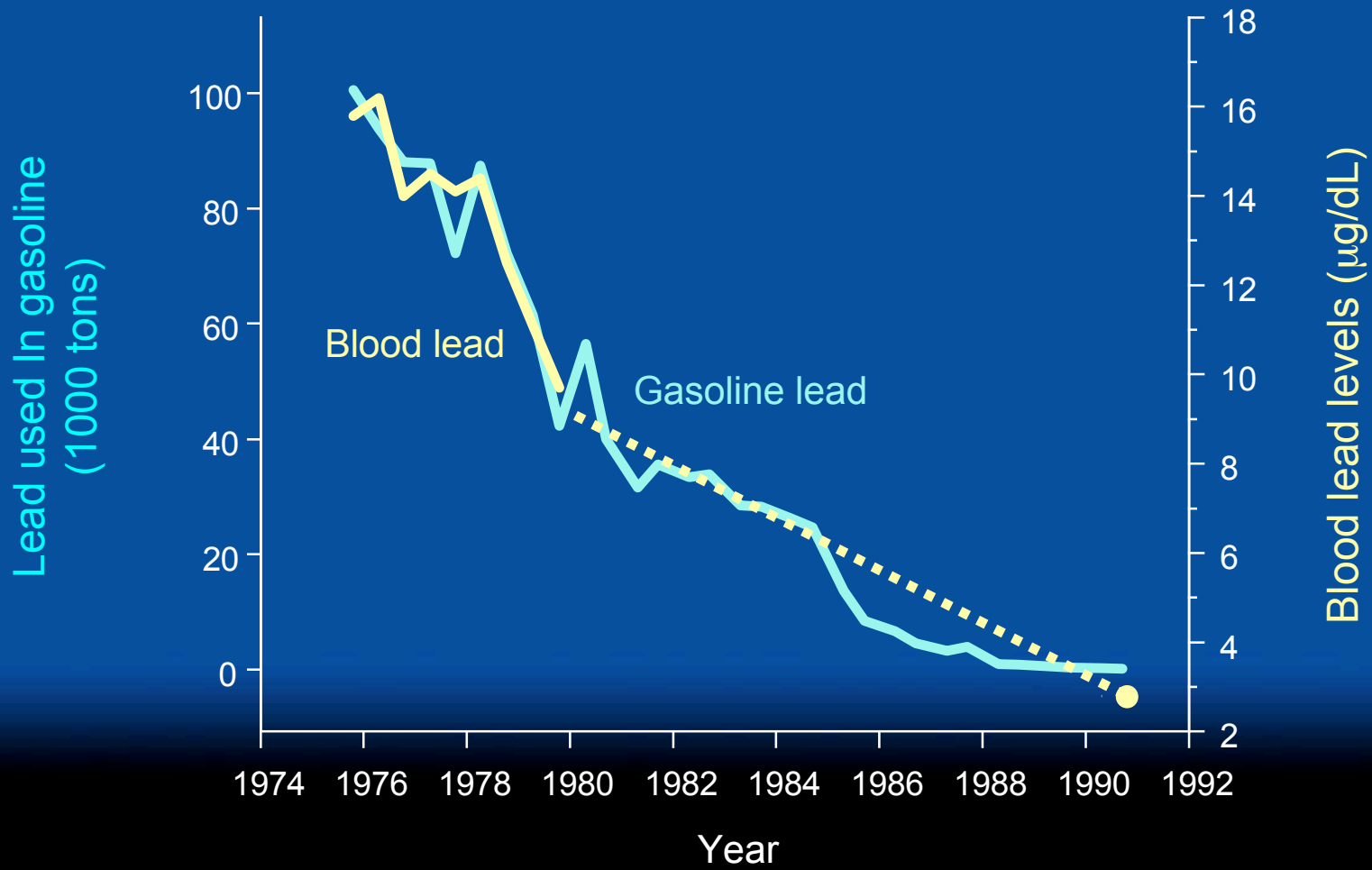
NHANES II Blood Lead Measurements Found A Substantial Decline in Blood Lead Levels, 10 Times More Than Predicted from Environmental Modeling



After NHANES II, EPA Further Restricted Leaded Gasoline and Gasoline Lead Levels Continued to Decline Through 1991

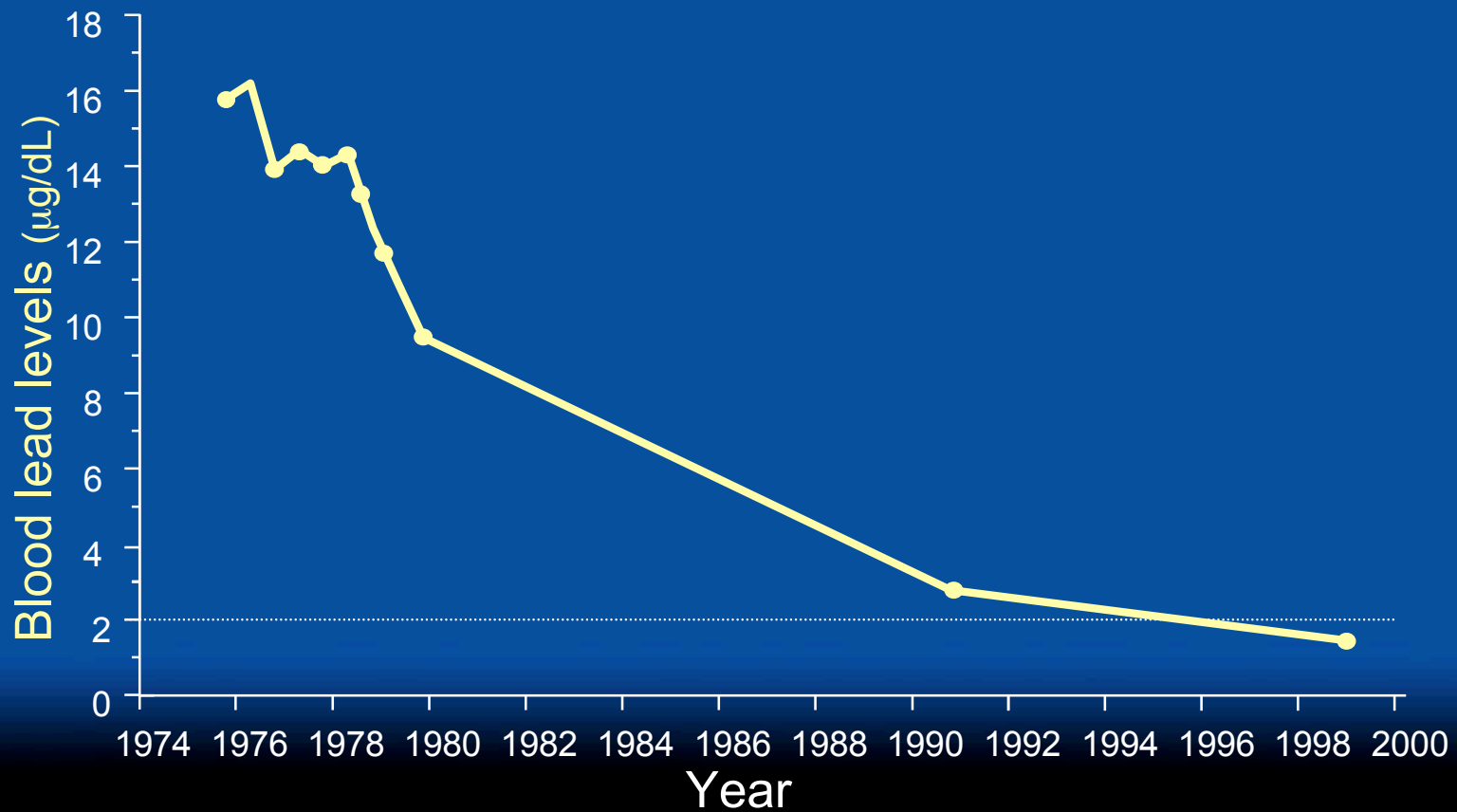


NHANES III (1988-1994) Showed Blood Lead Levels Continued to Decrease as Gasoline Levels Declined



Blood Lead Levels in the U.S. Population 1976 -2000

NHANES II, III, 1999-2000



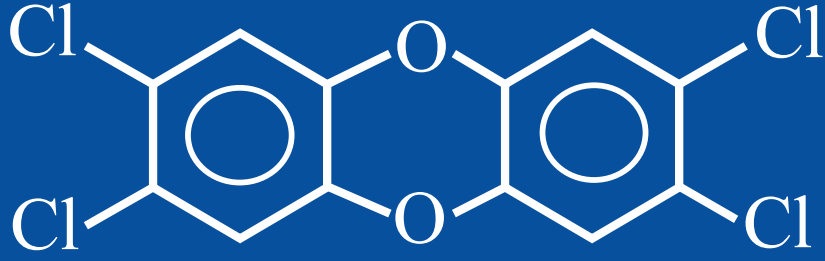
Major Findings: Decline in Blood Lead Levels among Children

For children 1 through 5 years old

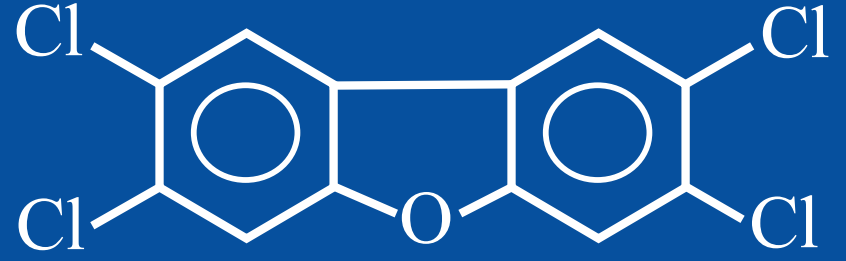
- NHANES III (1991-94)
 - ◆ Geometric mean BLL 2.7 $\mu\text{g}/\text{dL}$
 - ◆ 4.4% had BLLs $\geq 10 \mu\text{g}/\text{dL}$

- NHANES 1999-2000
 - ◆ Geometric mean BLL 2.23 $\mu\text{g}/\text{dL}$
 - ∨ 2.2% had BLLs $\geq 10 \mu\text{g}/\text{dL}$
 - ∨ Higher prevalence of BLLs in U.S. children occur in urban settings, lower SES, immigrants and refugees

(Geltman et al., 2001)

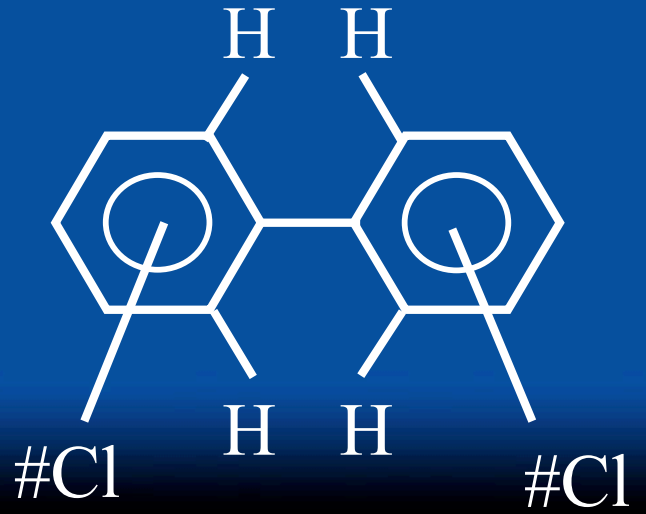


PCDDs

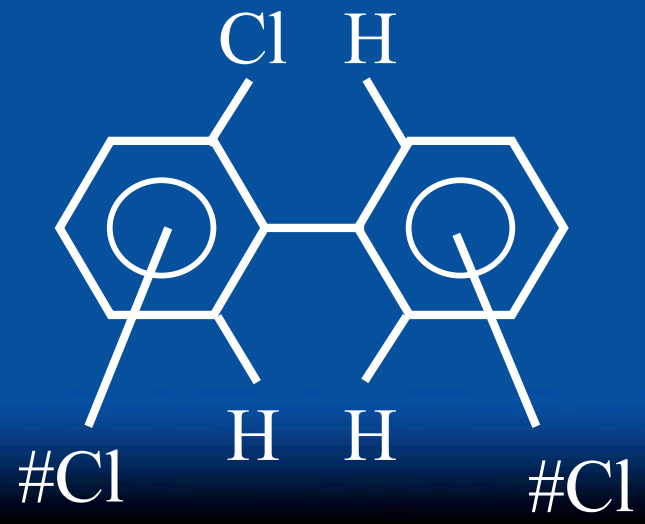


PCDFs

Dioxin-Like Chemicals



Coplanar Polychlorinated
Biphenyls

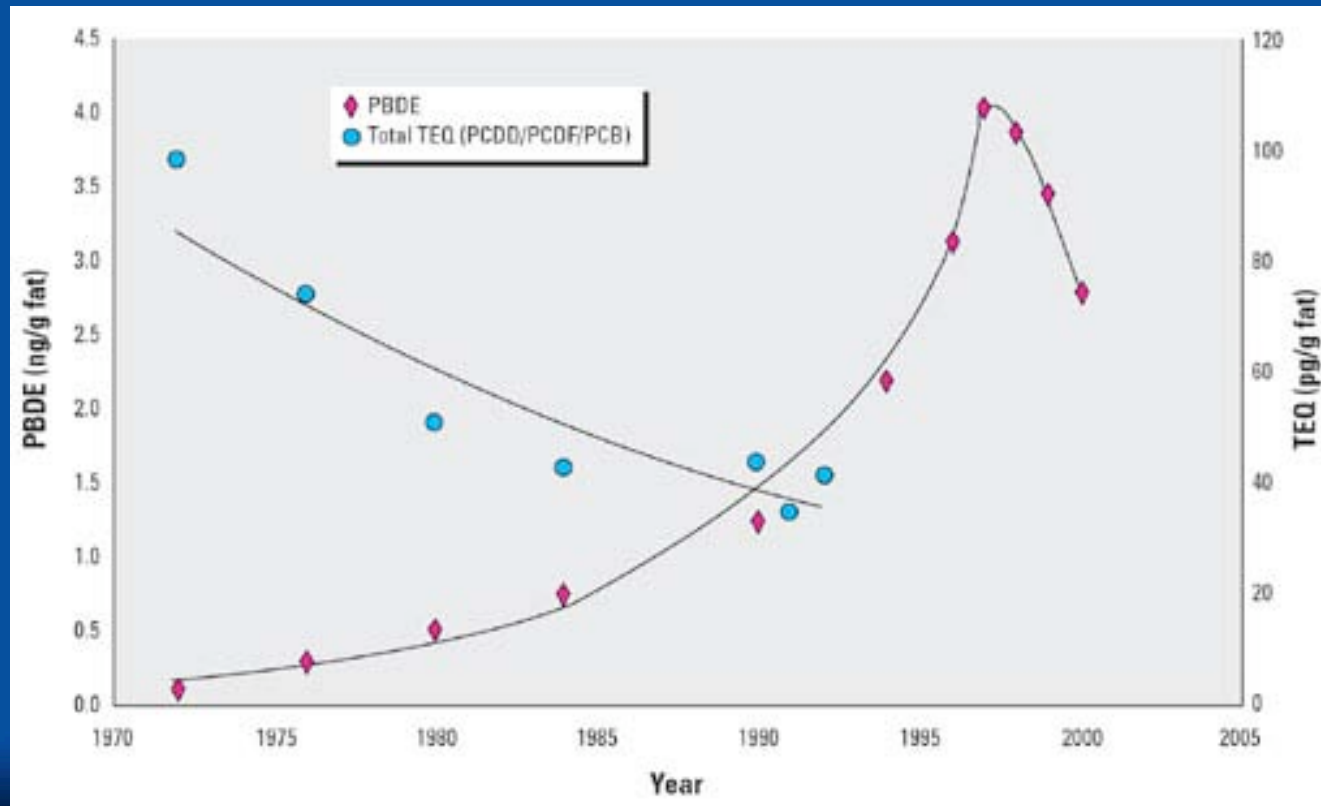


Mono-ortho-chlorinated
PCBs

Distribution and Storage of Dioxin-like Chemicals

- Because they are lipophilic, they tend to “travel” with lipids
 - ◆ Lipid Content
 - ★ Blood Serum ~0.6%
 - ★ Mother’s milk 3-4%
 - ★ Adipose tissue ~95%
- Therefore, need to adjust for lipid content in biological matrix

Organohalogen Compounds in Breast Milk in Sweden



Hooper and She, EHP 111(1): 109-114 (2003). Data from Noren and Mieronyte, 1998 and Guvenius and Noren, 2001

NHANES 1999-2000

Age \geq 20 years

Dioxin concentration data: Age Range (5th,
50th, 95th): 21, 42, 76 years

N \approx 1300

Serum \approx 5 mL per person

NHANES 1999-2000

PCDDs, PCDFs, PCBs – 95th Percentile

- Age 20 years and older (median age = 42 years)
- PCBs (total): ~2.7 ng/g serum
- Dioxin TEQ: 40-50 pg/g lipid
 - PCDD ~ 42 %
 - PCDF ~ 16 %
 - PCBs (coplanar) ~ 19%
 - PCBs (mono-ortho) ~ 23%

95th Percentile Dioxin TEQ Concentrations. NHANES 1999-2000

TEQ = 40-50 pg/g lipids*

N = 105

Age Range (5th, 50th, and 95th) = 39, 71, 85 years

Needham et al. Neurotoxicology (2005) online

* Range dependent on method used for imputing concentrations < LOD

Serum Pools: NHANES 2001-2002

- 34 People per pool (Total 1,734 people; 51 pools)
- Unweighted; used for estimates of the “means”
- 0.75mL Serum per person
- 25.5 g Serum per pool
 - ◆ 2 g BFRs/PCBs/Persistent Pesticides
 - ◆ 22 g PCDDs/PCDFs/cPCBs; PCNs
 - ◆ 0.5 g Total Lipids
 - ◆ 0.4 g Perfluorinated chemicals

Serum Pools: NHANES 2001-2002

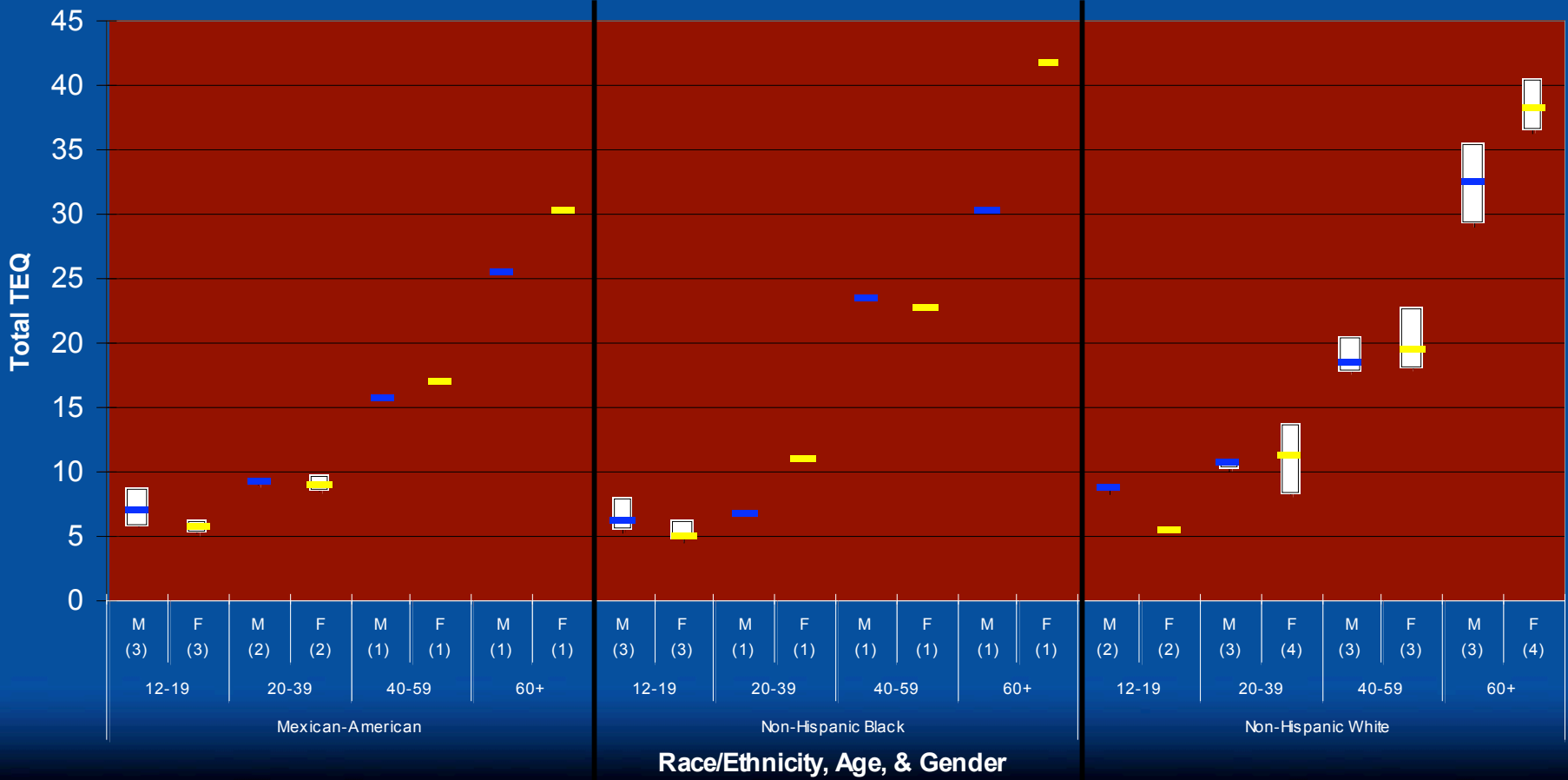
- Age, Race, Sex
- Note: Data do not include mono-ortho PCB concentrations

NHANES 2001-2002 Pools

Race/Ethnicity	Gender	Age Group (years)			
		Number of Pools			
		12-19	20-39	40-59	60+
Non-Hispanic White	M	2 (3)	3	3	3 (4)
	F	2 (3)	4	3	4
Non-Hispanic Black	M	3	1	1	1
	F	3	1	1	1
Mexican-American	M	3	2	1	1
	F	4	2	1	1

() for perfluorinated chemicals

Mean and Range of TEQs by Age Group, Race and Sex



Perfluorochemicals (PFCs) in the Environment

- Produced since 1950's for use in:
 - ◆ Surface treatments: soil and stain resistant coatings on textiles, carpet, leather
 - ◆ Paper protection: provides oil, grease and water resistance on paper products including those for food use
 - ◆ Performance chemicals including insecticide, fire fighting foams, industrial surfactants, acid mist suppression
- 3M phased out its fluorochemistry in May 2000

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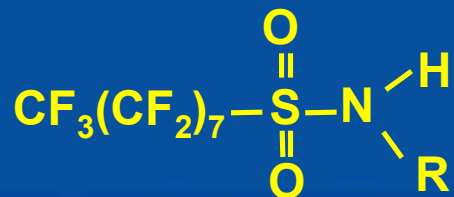
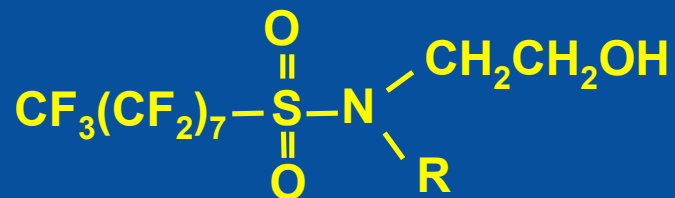
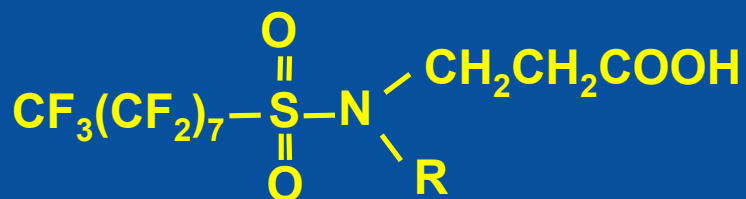
Some Potential Sources of Perfluorochemicals in the Environment

- Packaging materials
 - ◆ Food contact
- Stain-resistant coatings on textiles, carpet & leather
- Fire fighting foams
- Pesticides
- Dietary sources
- Degradation products
 - ◆ Perfluorooctanyl compounds
 - ◆ Fluoropolymers (e.g., telomers)

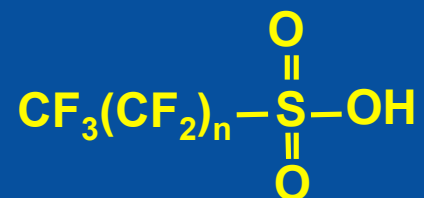


Perfluorinated Chemicals

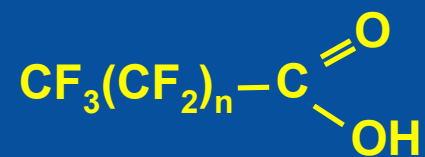
Sulfonamides



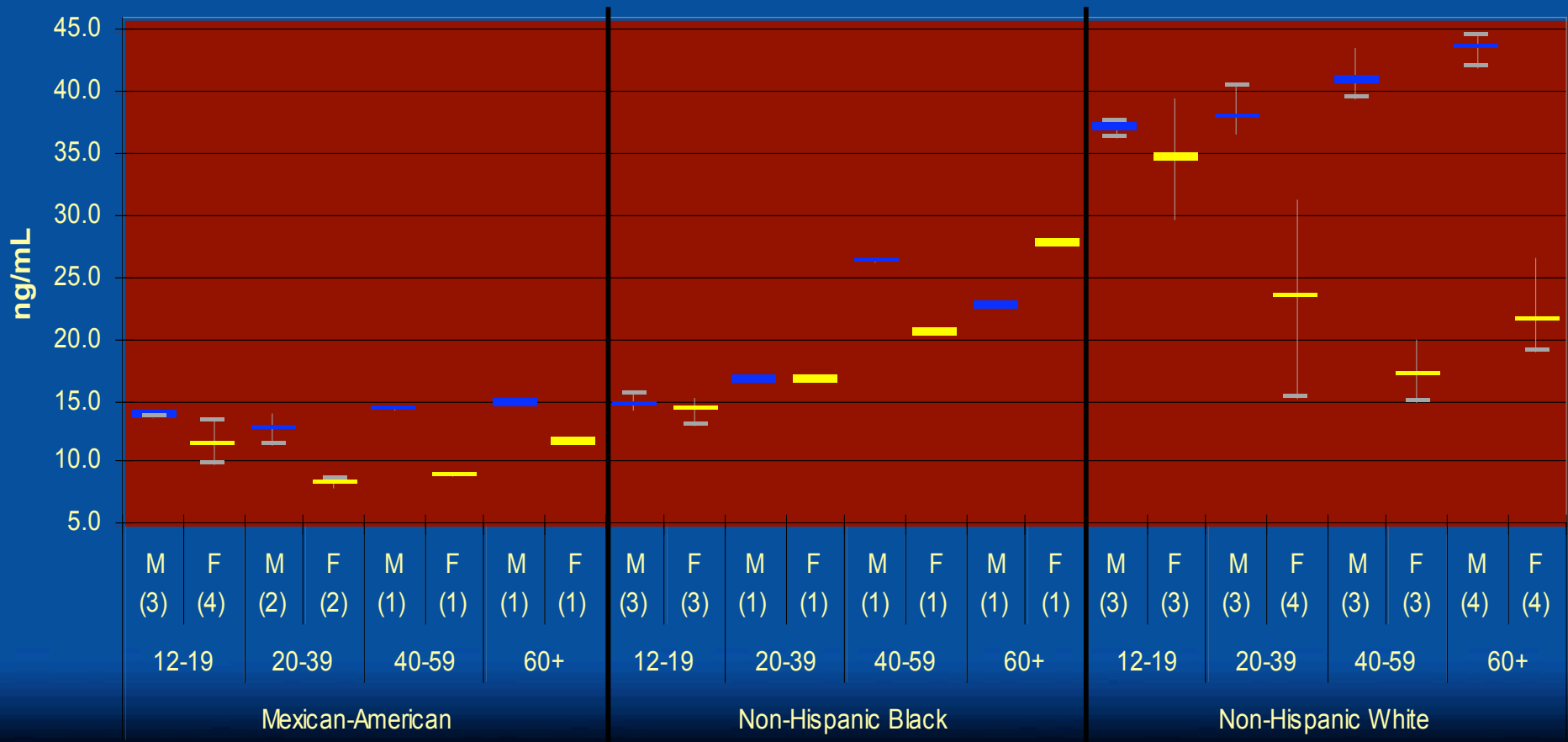
Sulfonic acids (e.g., PFOS)



Carboxylic acids (e.g., PFOA)

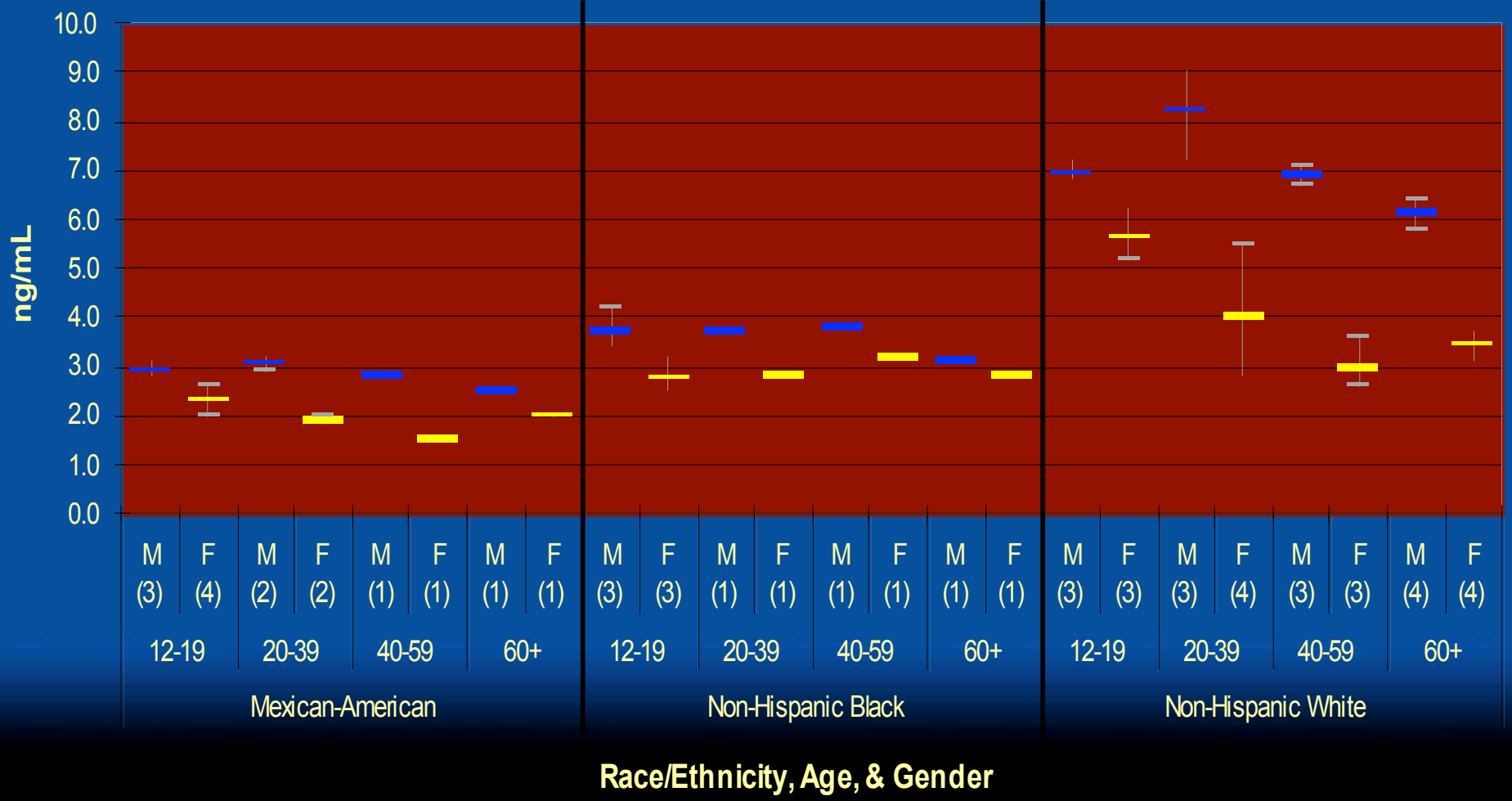


Mean and Range of PFOS by Age Group, Race and Sex



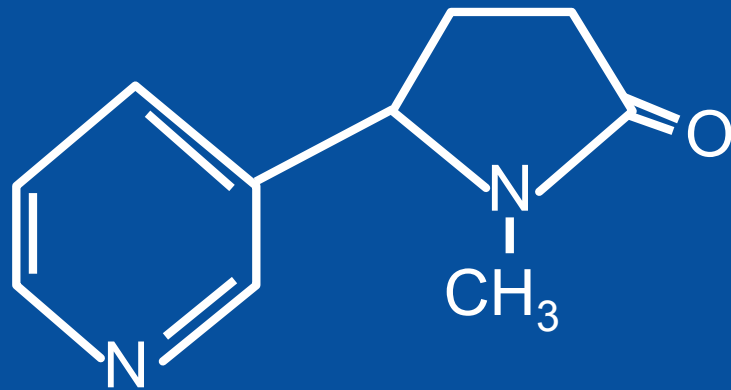
Race/Ethnicity, Age, & Gender

Mean and Range of PFOA by Age Group, Race and Sex

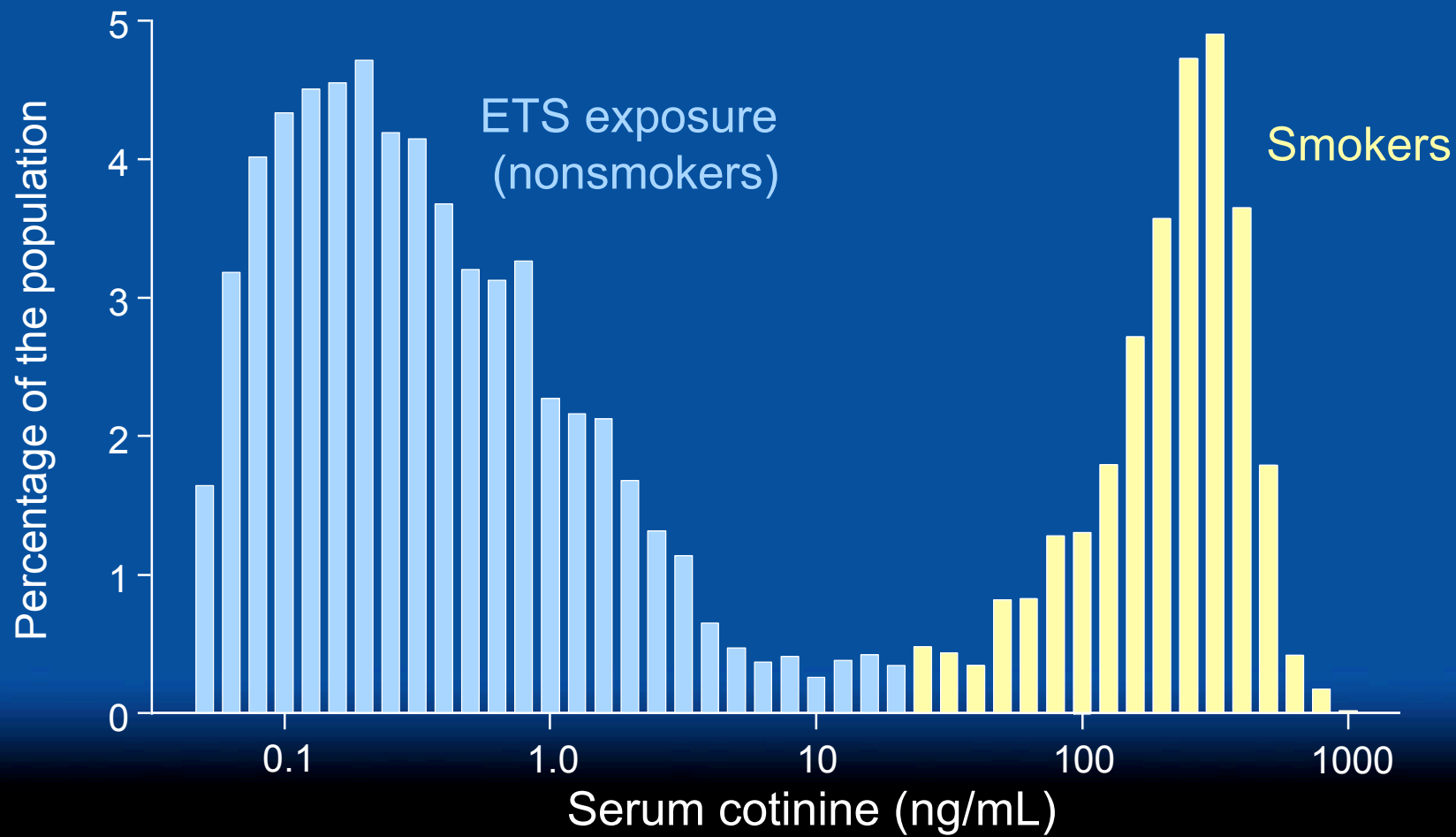


Cotinine

- Nicotine metabolite that tracks exposure to tobacco smoke
- For nonsmokers, tracks exposure to secondhand smoke



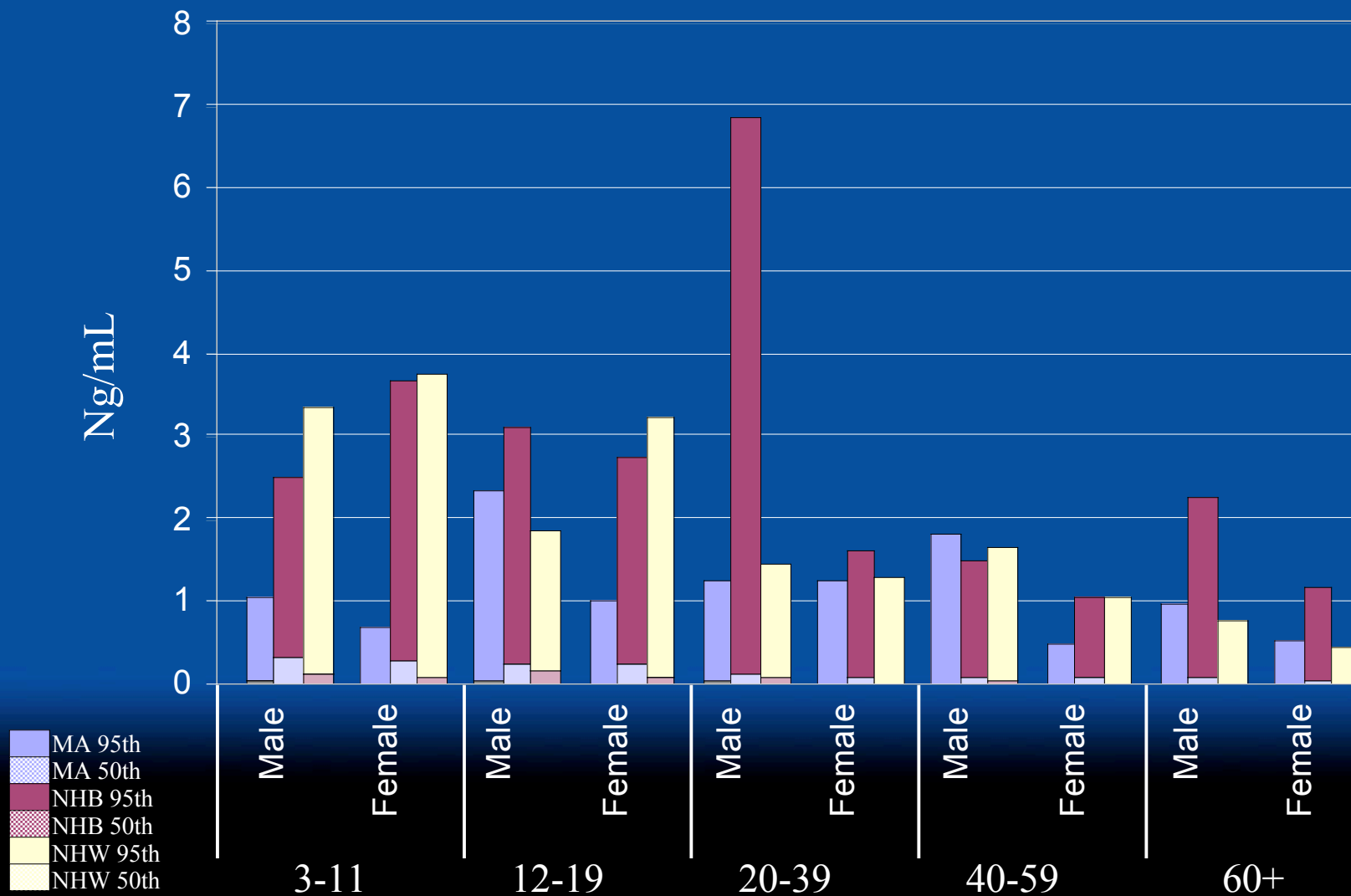
Exposure of the U.S. Population to Tobacco Smoke: Serum Cotinine Levels (NHANES III, 1988-1991)



Second Report Results

- Decrease in ETS 1988-1991 to 1999-2000
 - ◆ Measured as serum cotinine
 - ◆ Children: 58% decreased
 - ◆ Adolescents: 55% decreased
 - ◆ Adults: 75% decreased

50th & 95th Percentile of Cotinine by Age Group, Race & Sex

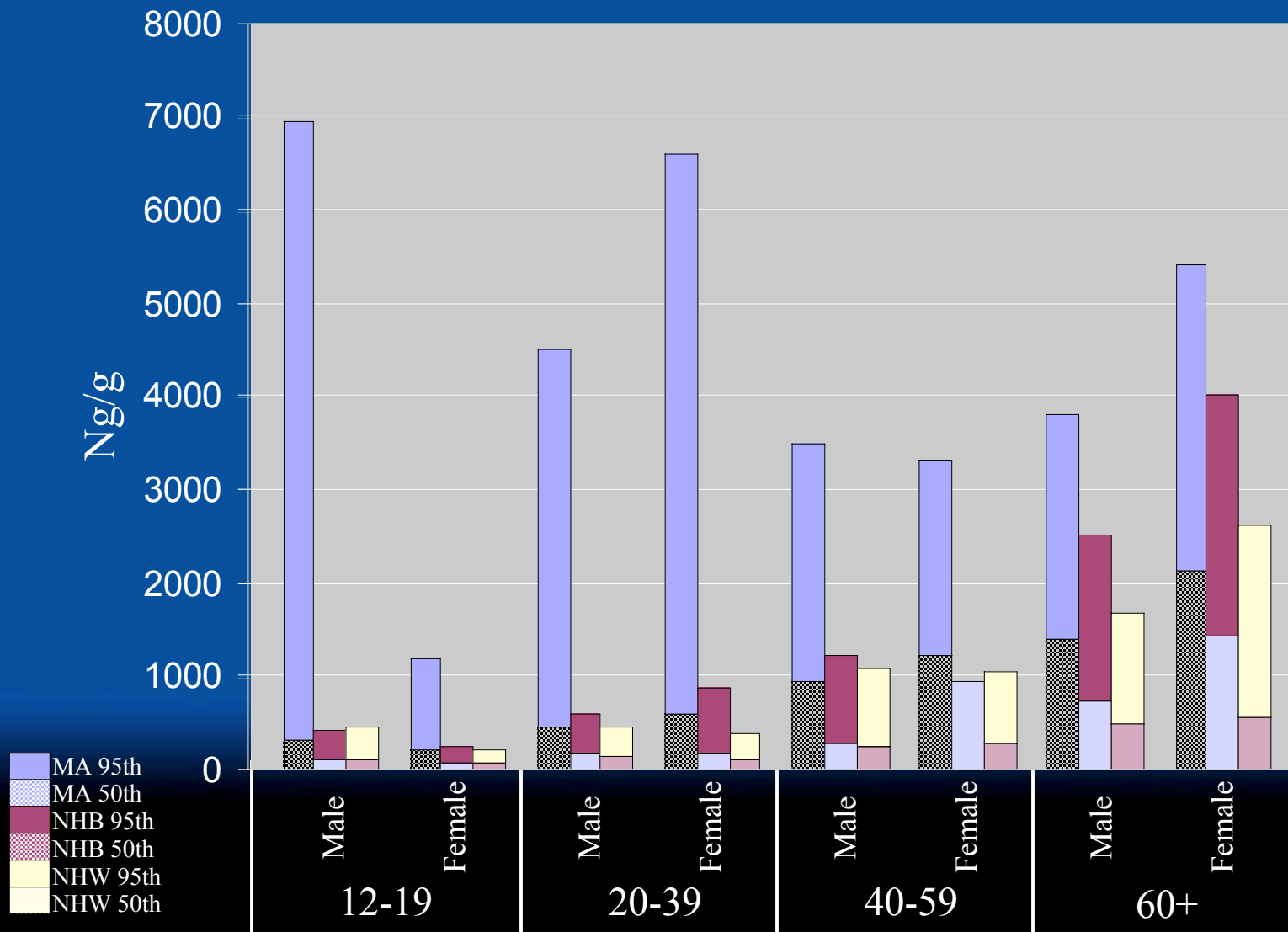


Second Report Results



- DDT banned in U.S. in 1973
- Pesticide DDE is 3 times higher in Mexican-Americans (3.9; 1.6; 1.3 ng/g)
- Also measurable in 12-19 year olds (born after ban) (0.6 vs. 1.8 ng/g)
- May be persisting in environment or from imported food

50th & 95th Percentile of DDE by Age Group, Race & Sex



Third *National Report* on Human Exposure to Environmental Chemicals

Includes chemicals from *Second National Report* (1999-2000)
+ the following in NHANES 2001-2002

- Organochlorine pesticides: aldrin, dieldrin, endrin
- OP pesticides: additional metabolites
- Pyrethroids: 5 metabolites
- Herbicides: mercapturate metabolites of acetochlor and metolachlor
- PAHs: 1-, 2-, and 4-hydroxychrysene; 4- and 9-hydroxyphenanthrene; 9-hydroxyfluorene; 3-hydroxybenzo(a)pyrene
- Additional PCDDs and PCBs
- Additional phthalate metabolites (e.g., oxidative metabolites of DEHP and DnOP)

Seveso, Italy Scenario

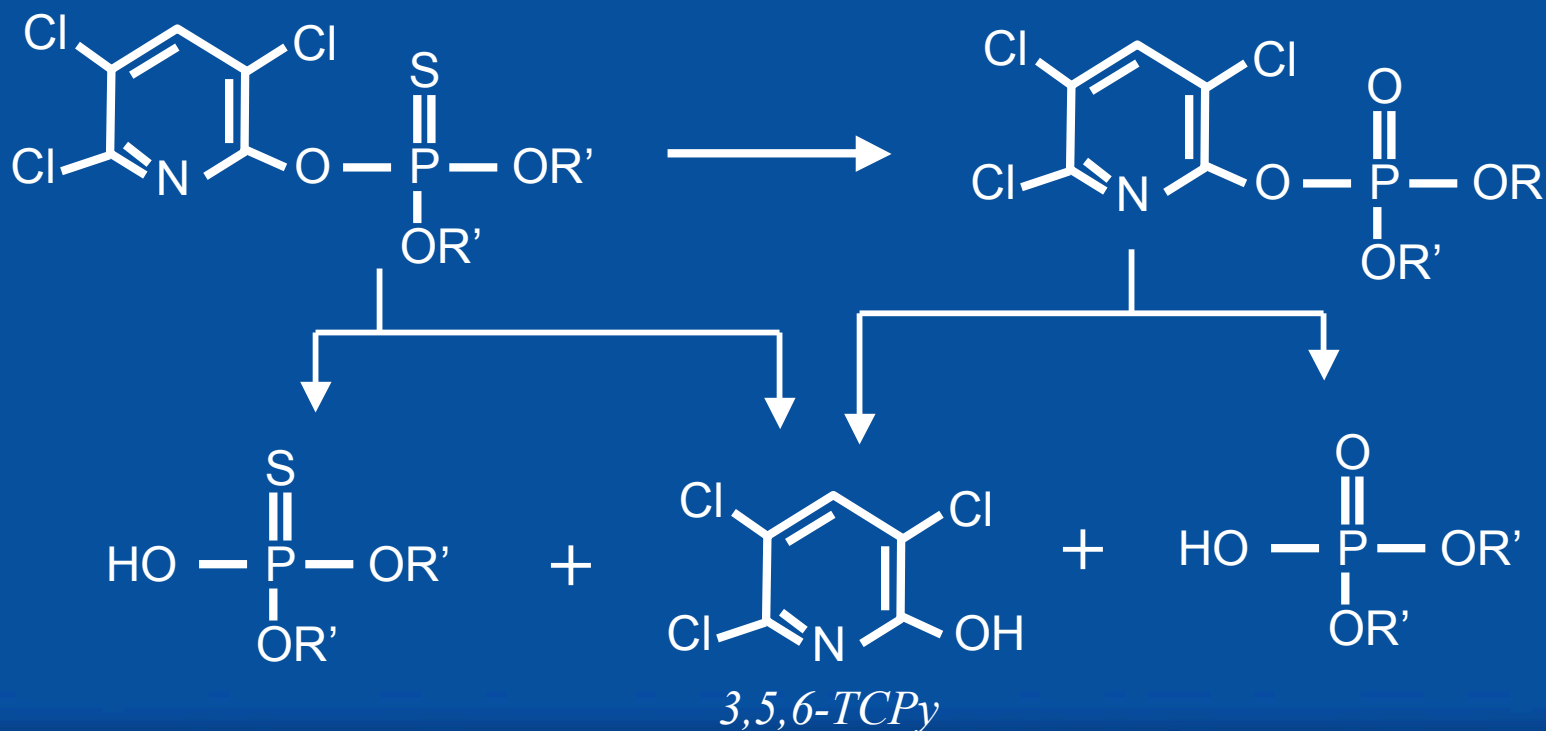
- Saturday – July 10, 1976
 - ◆ Explosion in a TCP reactor
 - ◆ Atmospheric release of kilogram amount of 2,3,7,8-TCDD
- People potentially exposed
 - ◆ A Zone – 736
 - ◆ B Zone – 4,737
 - ◆ R Zone – 31,800
- Highest measured level
 - ◆ 56,000 ppt (Oct. 1976)

Chlorpyrifos

- Organophosphorus pesticide
- Many food uses
- Termiticide
- Use in and around homes and non-residential settings - eliminated

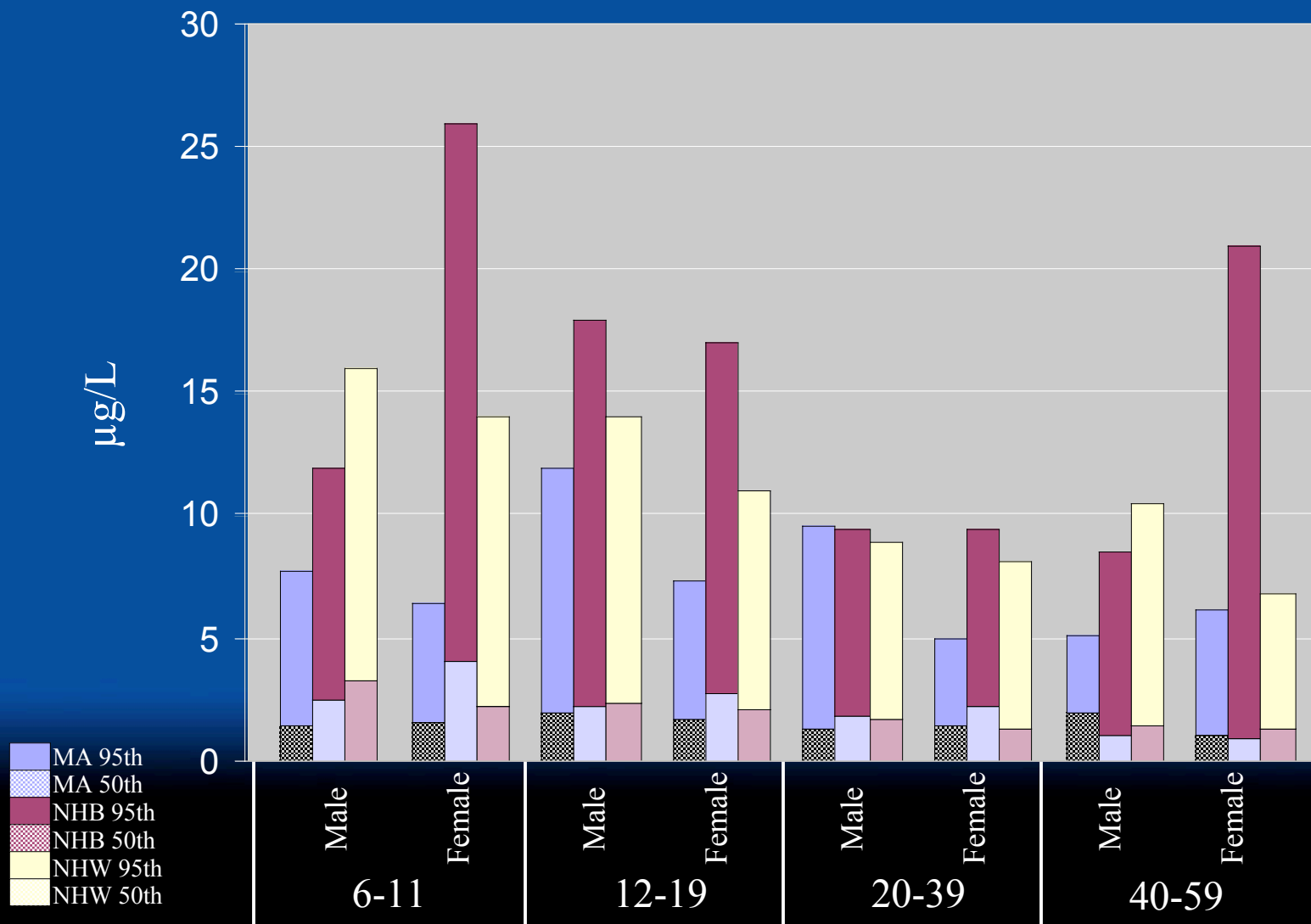
Limitation: Specificity of Analysis

Chlorpyrifos (R'=ethyl) and Chlorpyrifos-methyl (R'=methyl)
Metabolism and Env'l Degradation

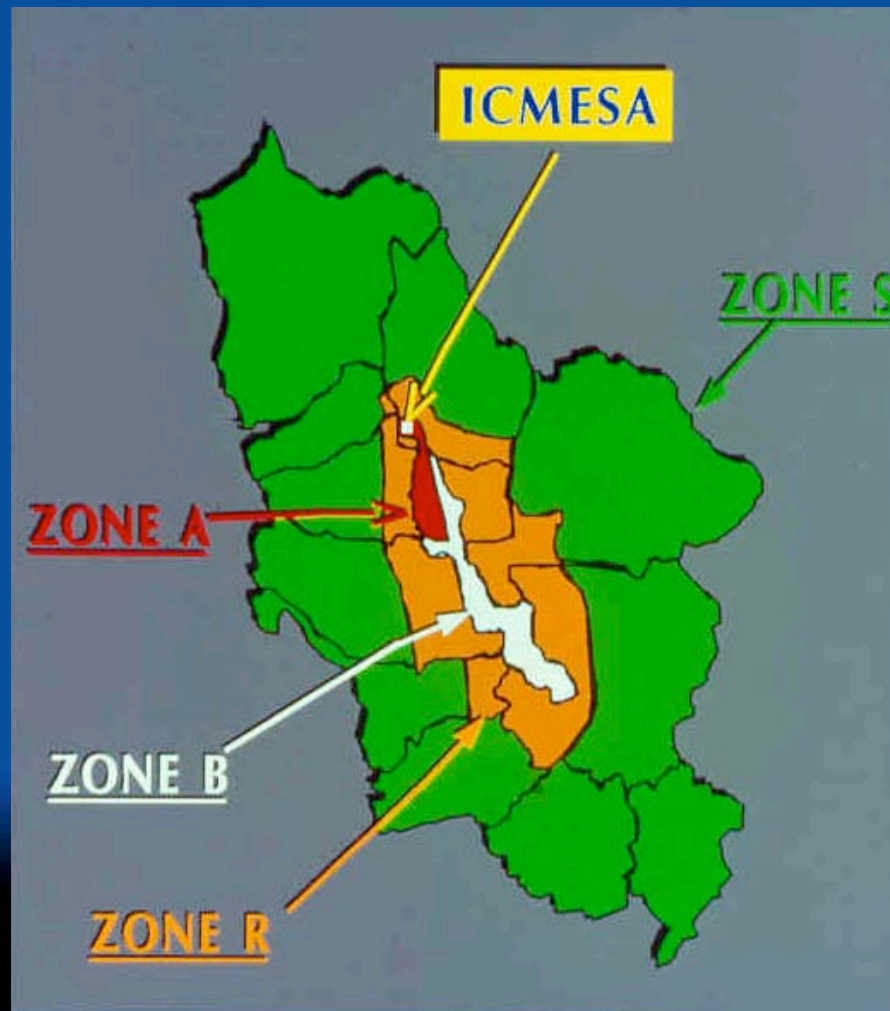


3,5,6-TCPy is “specific” metabolite
Dialkyl phosphates are “nonspecific” metabolites

50th & 95th Percentile of 3,5,6-TCPy by Age Group, Race & Sex



Map of Seveso Showing Contaminated Area

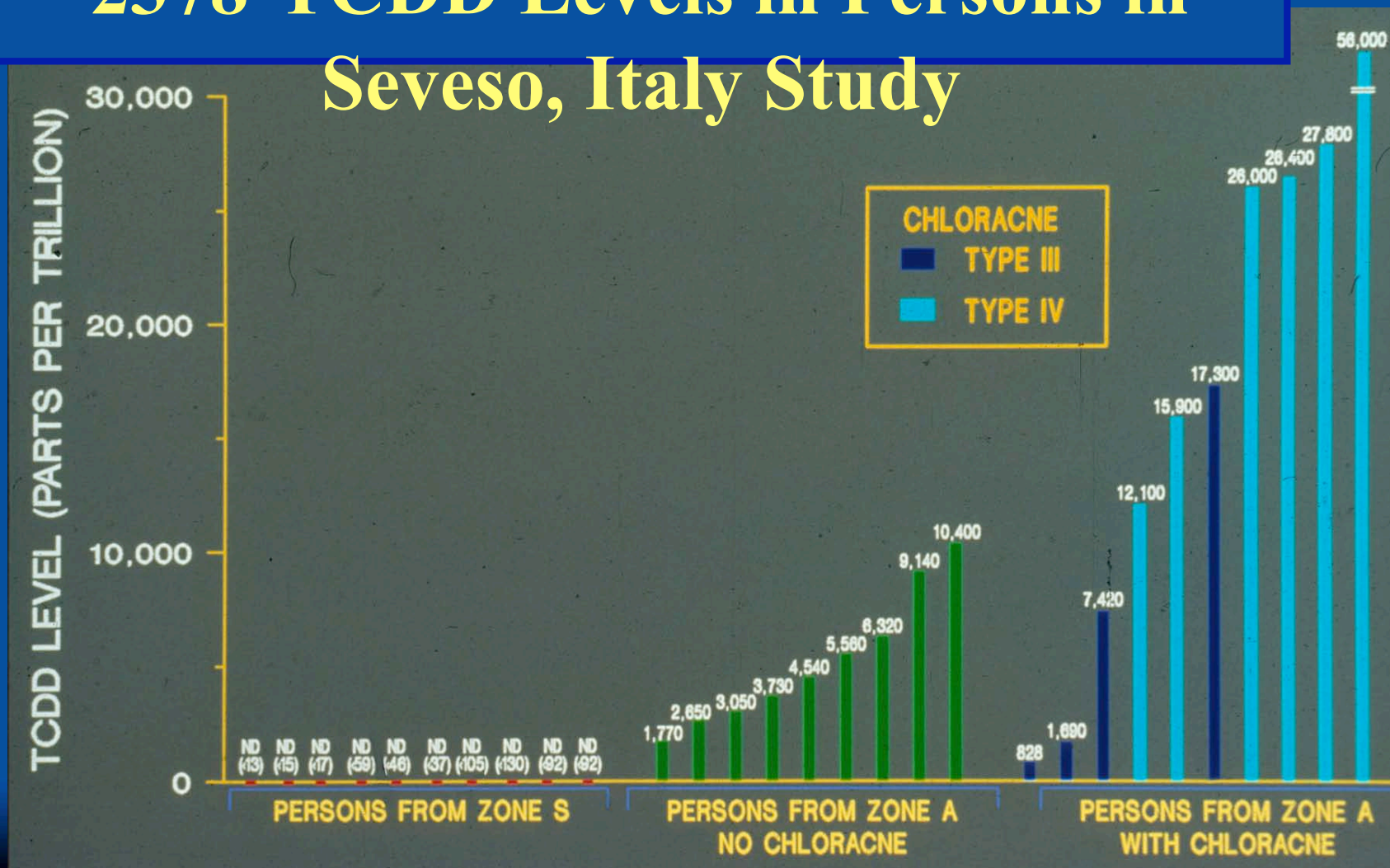




Seveso, Italy

- Acute exposure
- Wide range of exposure
- Both genders
- Adults and children
- Serum specimens saved from 1976-1985 medical exams

2378-TCDD Levels in Persons in Seveso, Italy Study



Mocarelli et al. *J Toxicol Environ Health* 32 (1991) 357-366.

Seveso, Italy: Serum TCDD Levels (1976) by Zone of Residence

Zone	Population	N	Range	Median
A	736	296	ND-56,000	447
B	4,737	80	ND-725	94
R	31,800	48	ND-545	48
Non ABR	182,843	11*	ND (<12)-169	15

*Pools of 4-10 individuals per pool

Needham et al. *Teratogenesis, Carcinogenesis & Mutagenesis* 17 (1997)
225-240.

Change in Sex Ratio with Exposure to Dioxin

- Seveso, Italy Dioxin Explosion
 - ◆ July 10, 1976 factory explosion
 - ◆ A Zone (736 people)
- Normal sex ratio (106 M and 100 F)

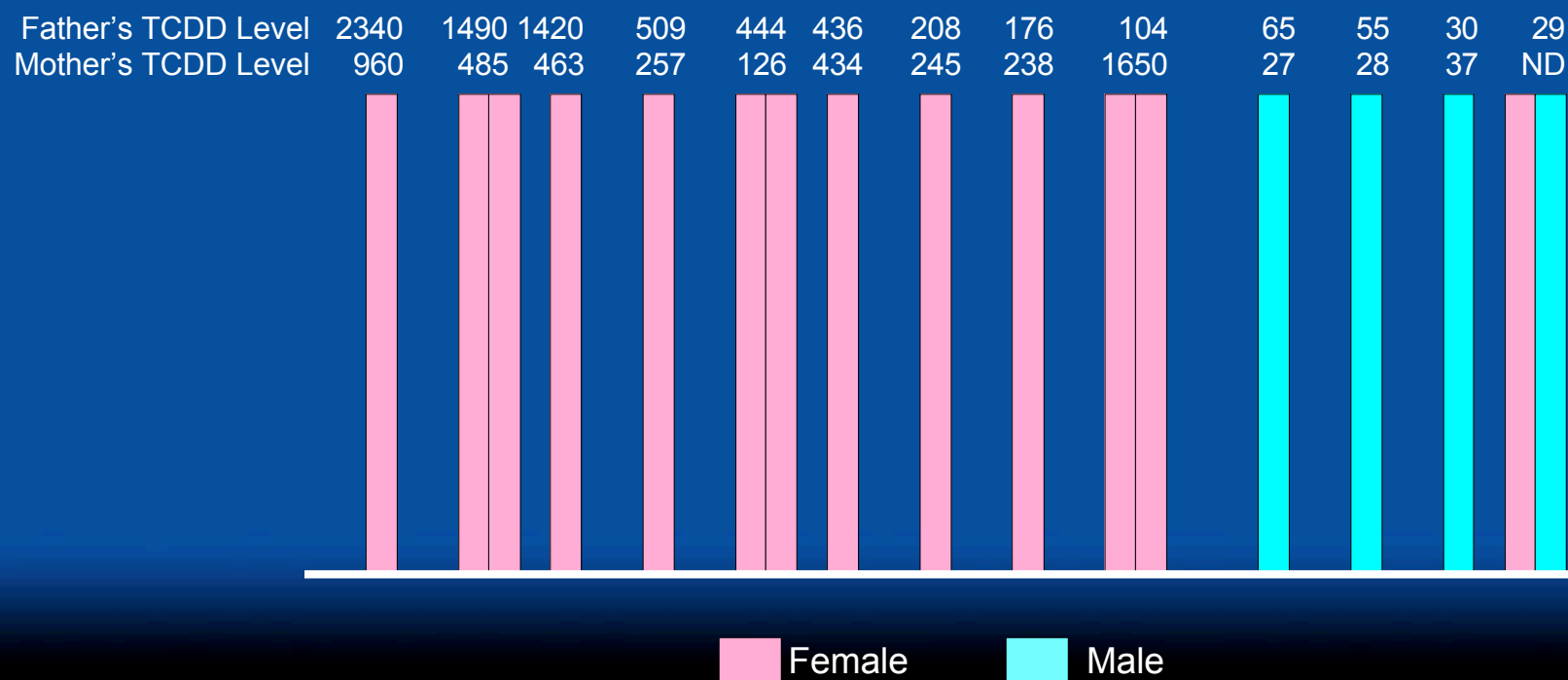
Mocarelli, Brambilla, Gerthoux, Patterson, Needham, *The Lancet*, 348:409 (1996)

Change in Sex Ratio with Exposure to Dioxin

- 74 Total births from 9 months after accident to December 1984 (~1 half-life of serum TCDD)
 - ◆ Excess of females (26 M vs. 48 F)
 - ◆ χ^2 (P < 0.001)
- From 1985 to 1994
 - ◆ 60 Males and 64 Females

Mocarelli, Brambilla, Gerthoux, Patterson, Needham, *The Lancet*, 348:409 (1996)

Sex Distribution of Children Born April 1977 – December 1984 to Parents with Measured Serum TCDD Levels (ppt) in Zone A – Seveso, Italy



Needham et al. Teratogenesis, Carcinogenesis, and Mutagenesis. 17:225-240 (1997).