Biomonitoring: An Integral Part of Exposure Analysis

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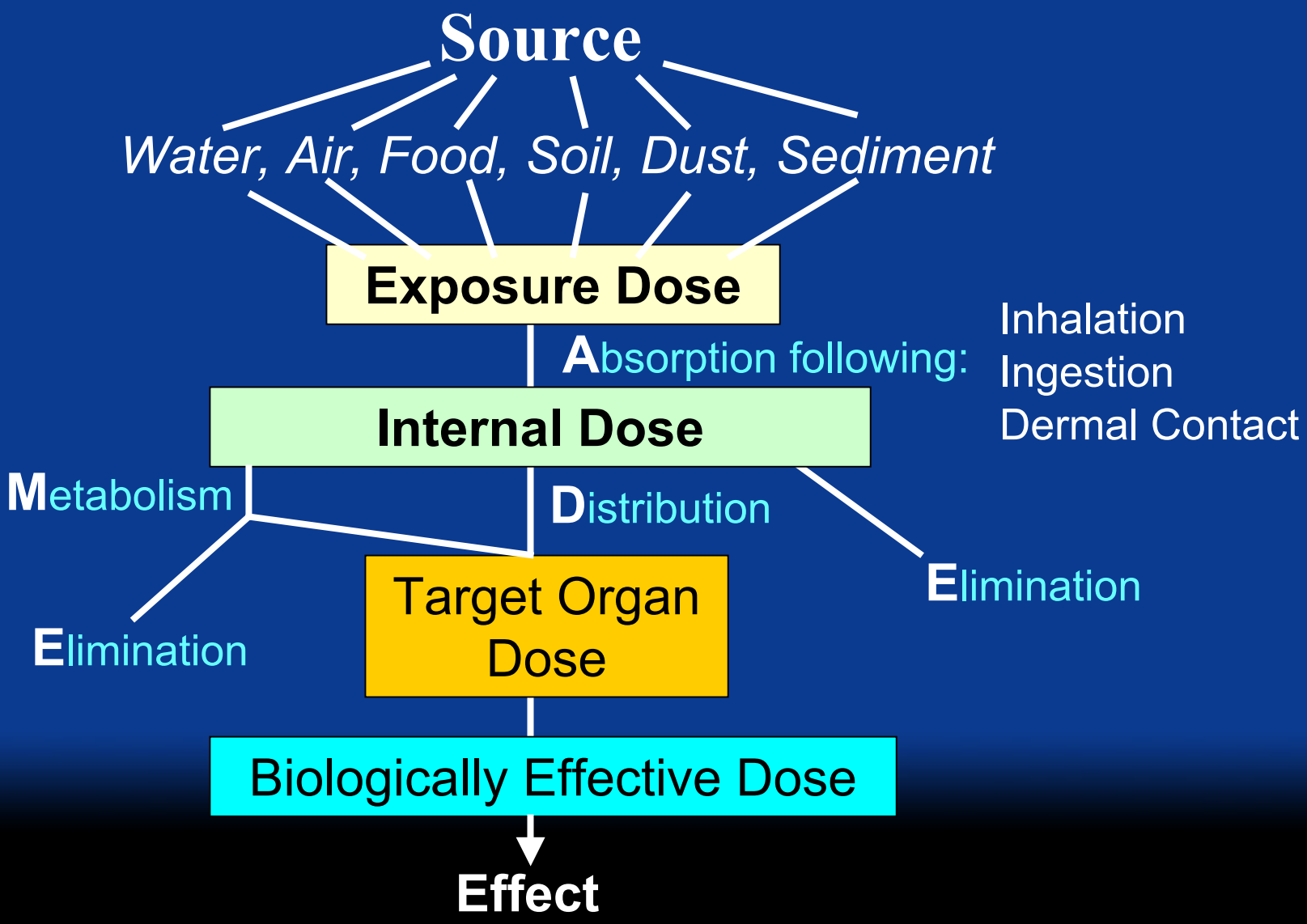
Biomonitoring

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.

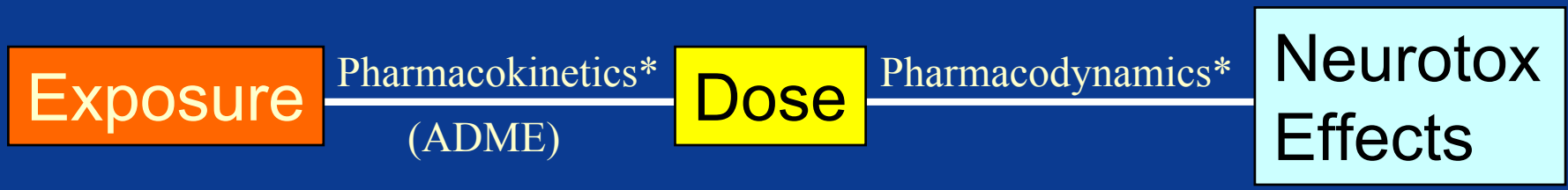
Exposure Pathway



How Do We Assess Exposure?

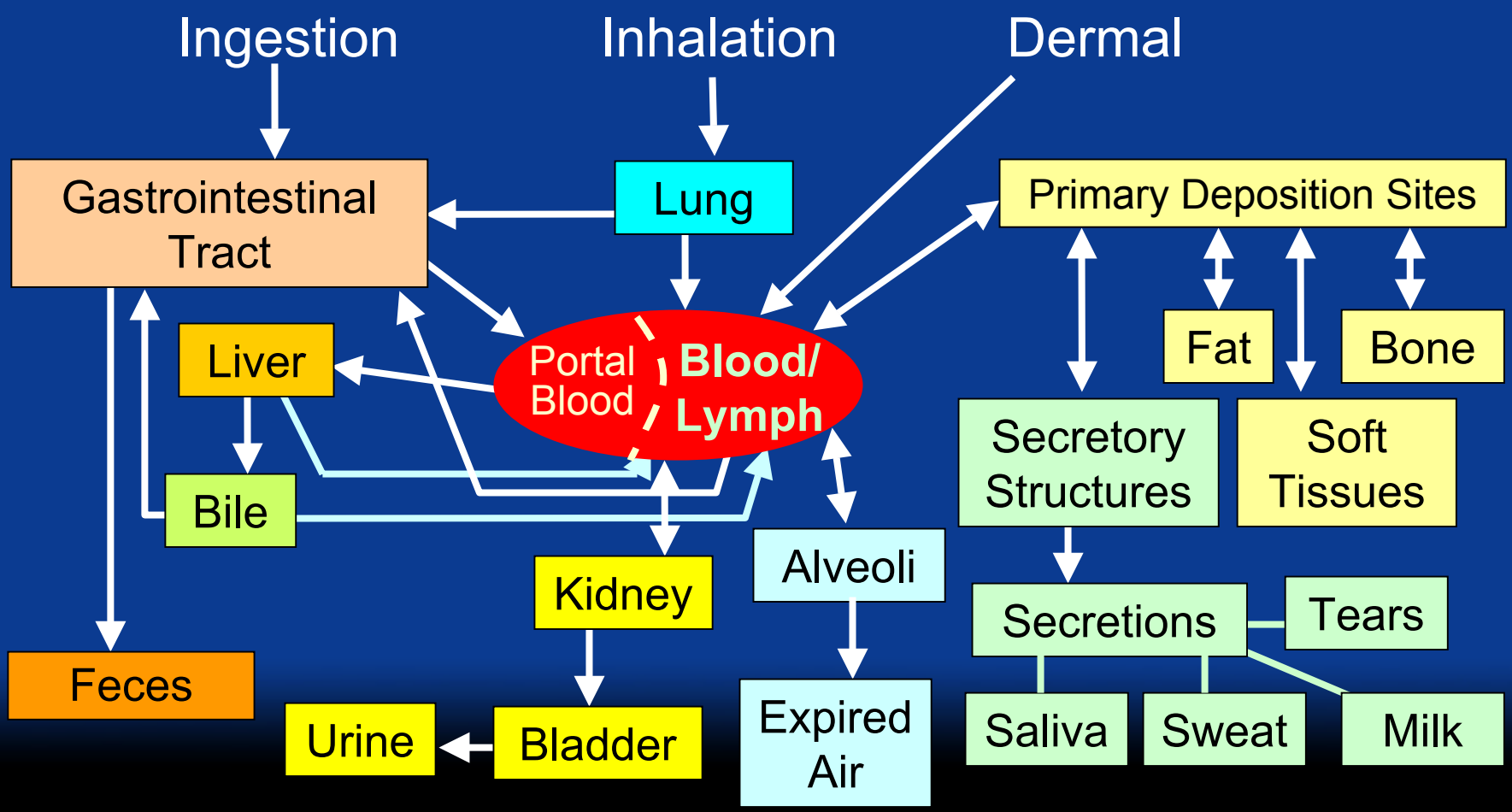
- Questionnaires including diaries and videotaping
- Environmental measurements
- Biomonitoring (uptake)

Predicting Adverse Health Outcomes Following Human Exposure to Environmental Chemicals is Problematic or "Why do people respond differently to similar exposures?"

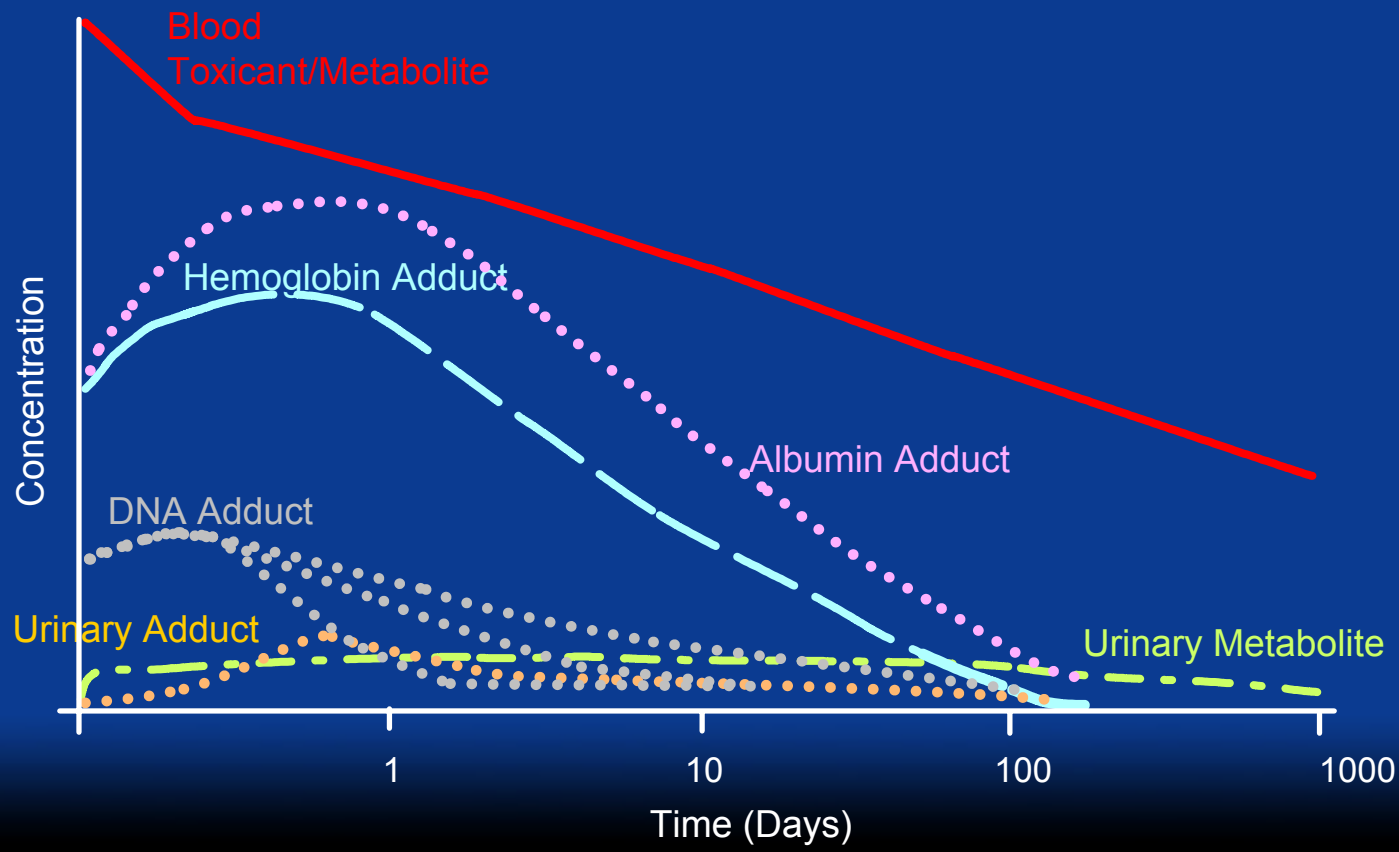


*
- Genetic factors
- Demographic factors (age, sex, geography)
- Environmental and behavioral stressors
- Nutritional status
- Other exposures

Pharmacokinetics of Environmental Chemicals in Body and What Matrices Are Available for Analyses

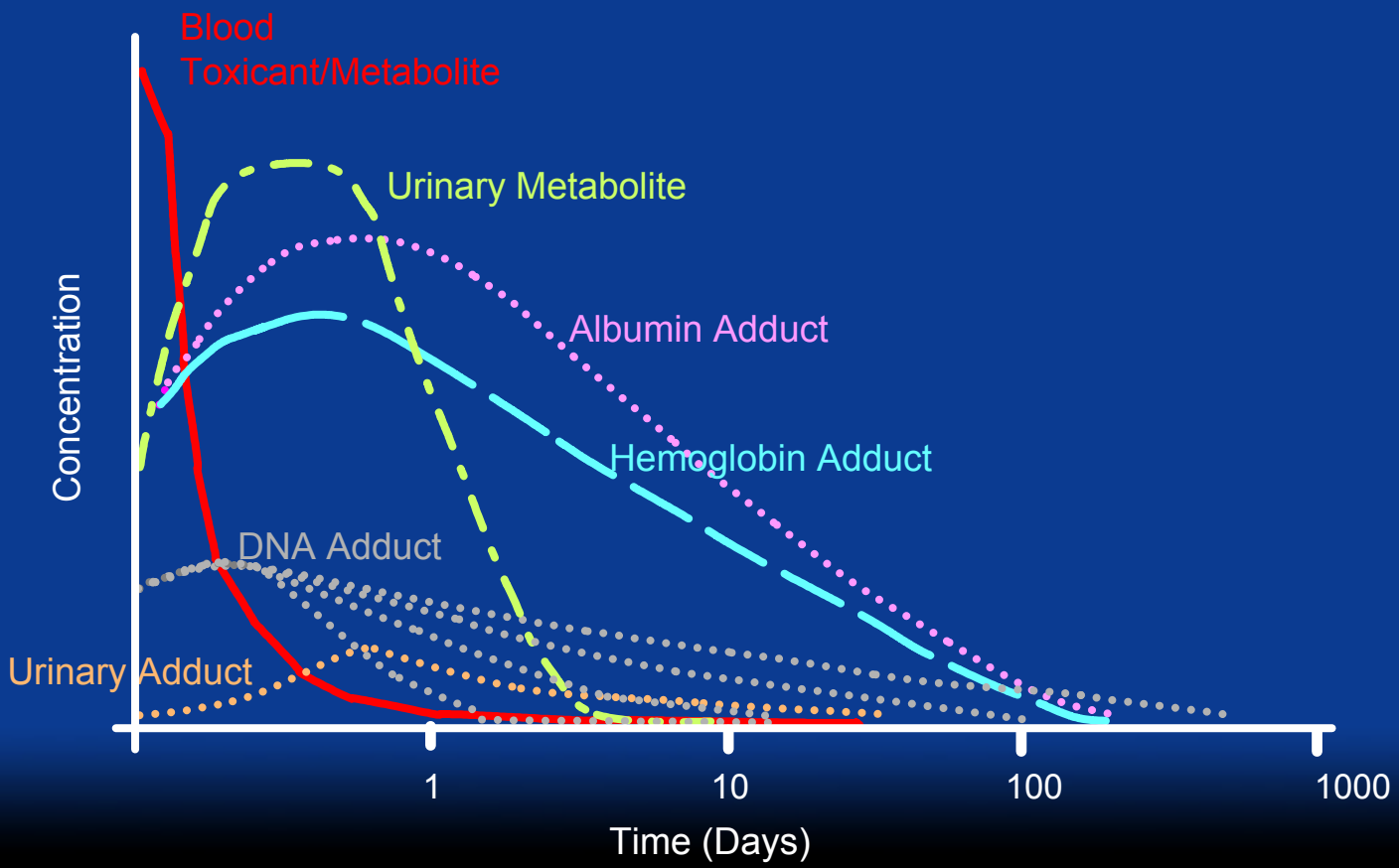


Post-Exposure Fate of a Persistent Chemical in Blood and Urine



Needham and Sexton, JEAEE **10**:611-629 (2000)

Post-Exposure Fate of a Nonpersistent Chemical in Blood and Urine



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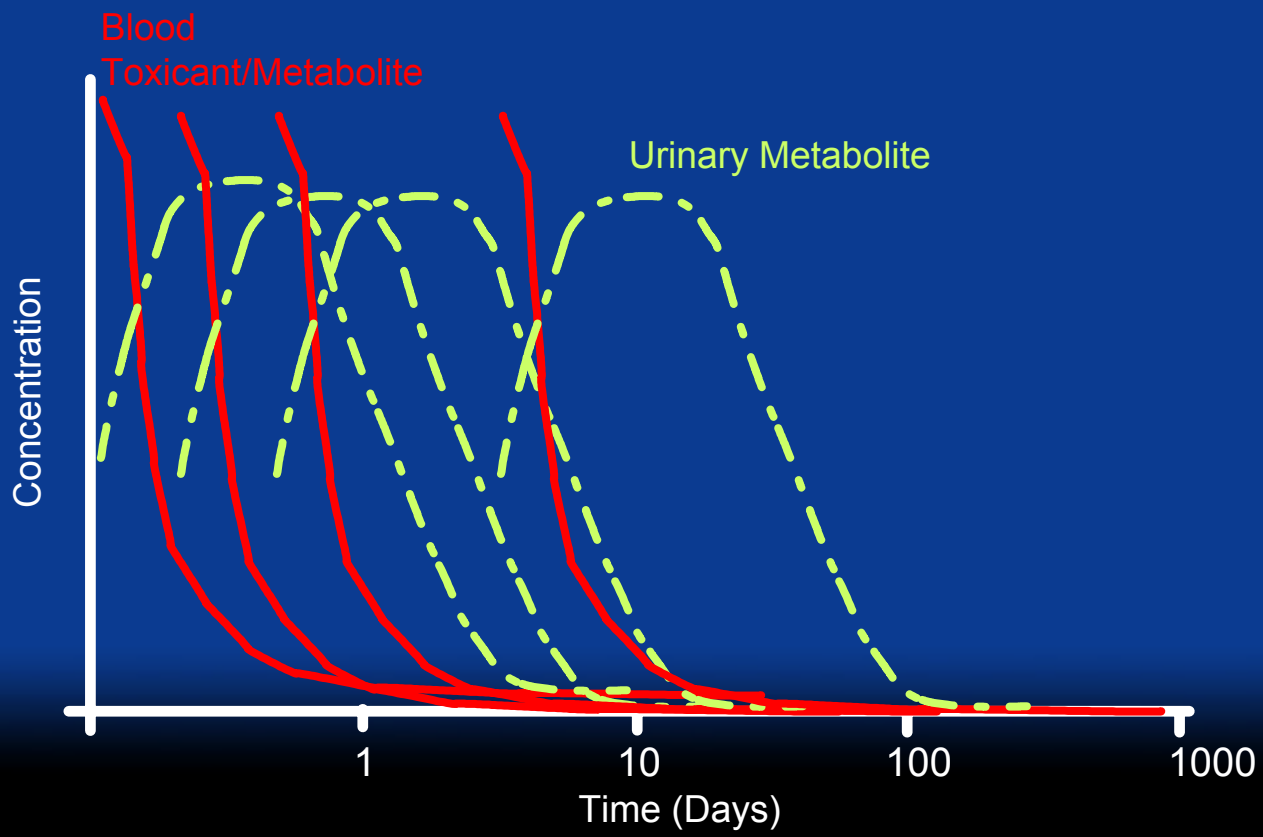


Urine

Metals (13)

PAH metabolites

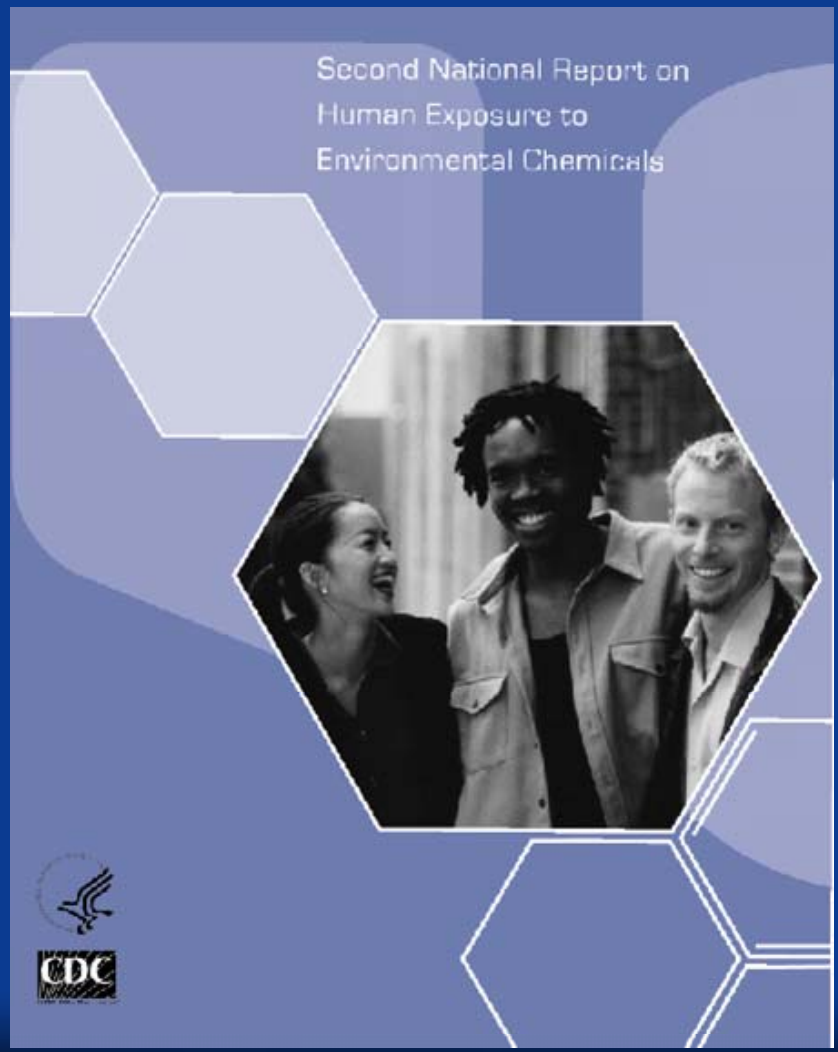
Phthalate metabolites

Pesticides

- Organophosphorus
- Carbamates
- Herbicides

Repellants

Phytoestrogens



Blood

Lead

Cadmium

Mercury

Serum

Dioxins

Furans

PCBs

Organochlorine pesticides

Cotinine

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
- 10^{th}, 25^{th}, 50^{th}, 75^{th}, 90^{th}, and 95^{th} 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: www.cdc.gov/nchs/nhanes/htm

National Report on Human Exposure to Environmental Chemicals

Urine Specimens	Ages ≥ 6 y
Blood Specimens	Ages ≥ 12 y

Exceptions: Pb, Cd, Hg, cotinine

Interpreting Data in the Report

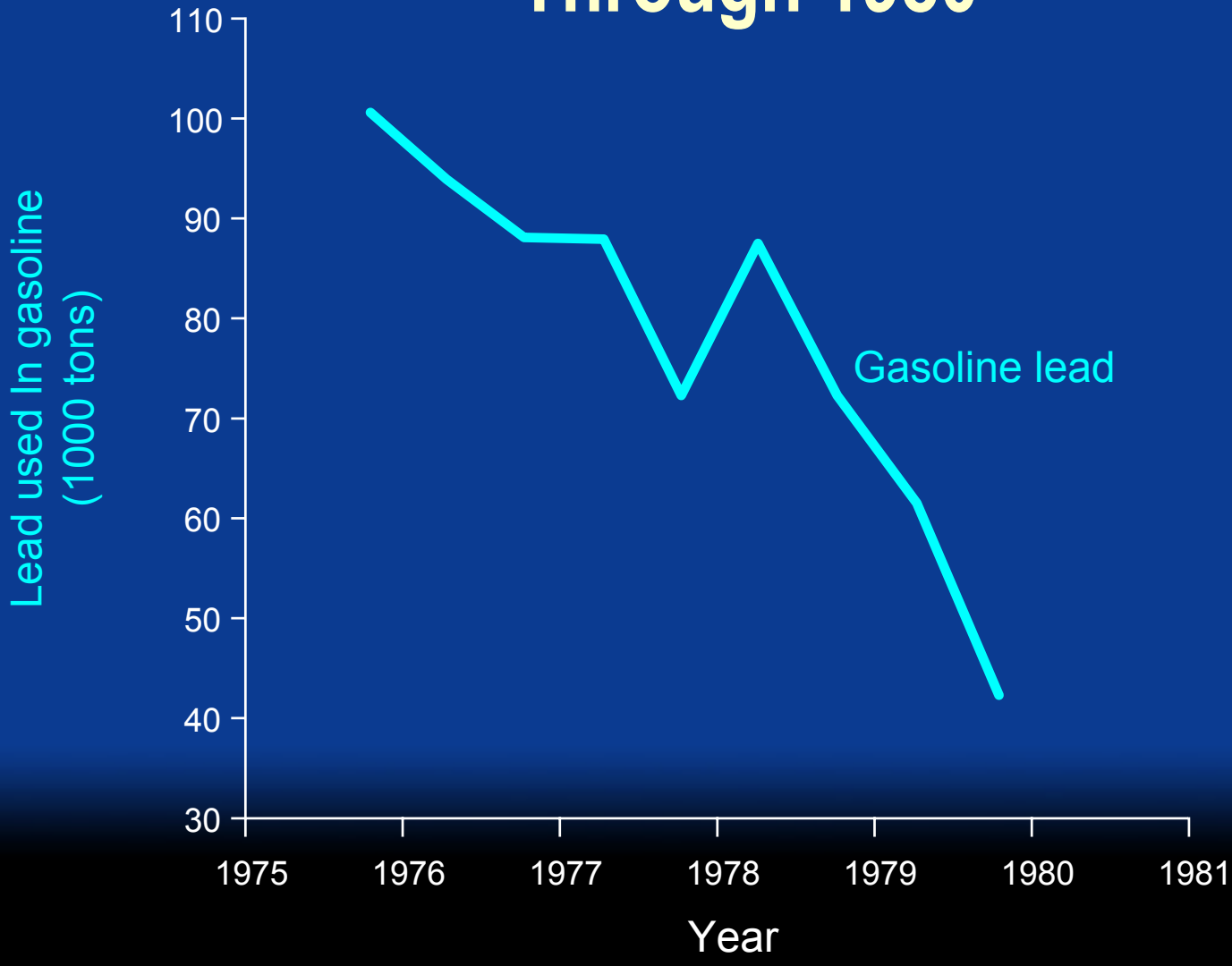
- The presence of a chemical in the body does not mean it causes disease
- For many chemicals in the Report, more research is needed to interpret these levels
- The report provides new exposure data, but does not identify levels that cause disease
  - Additional studies are needed

Lead

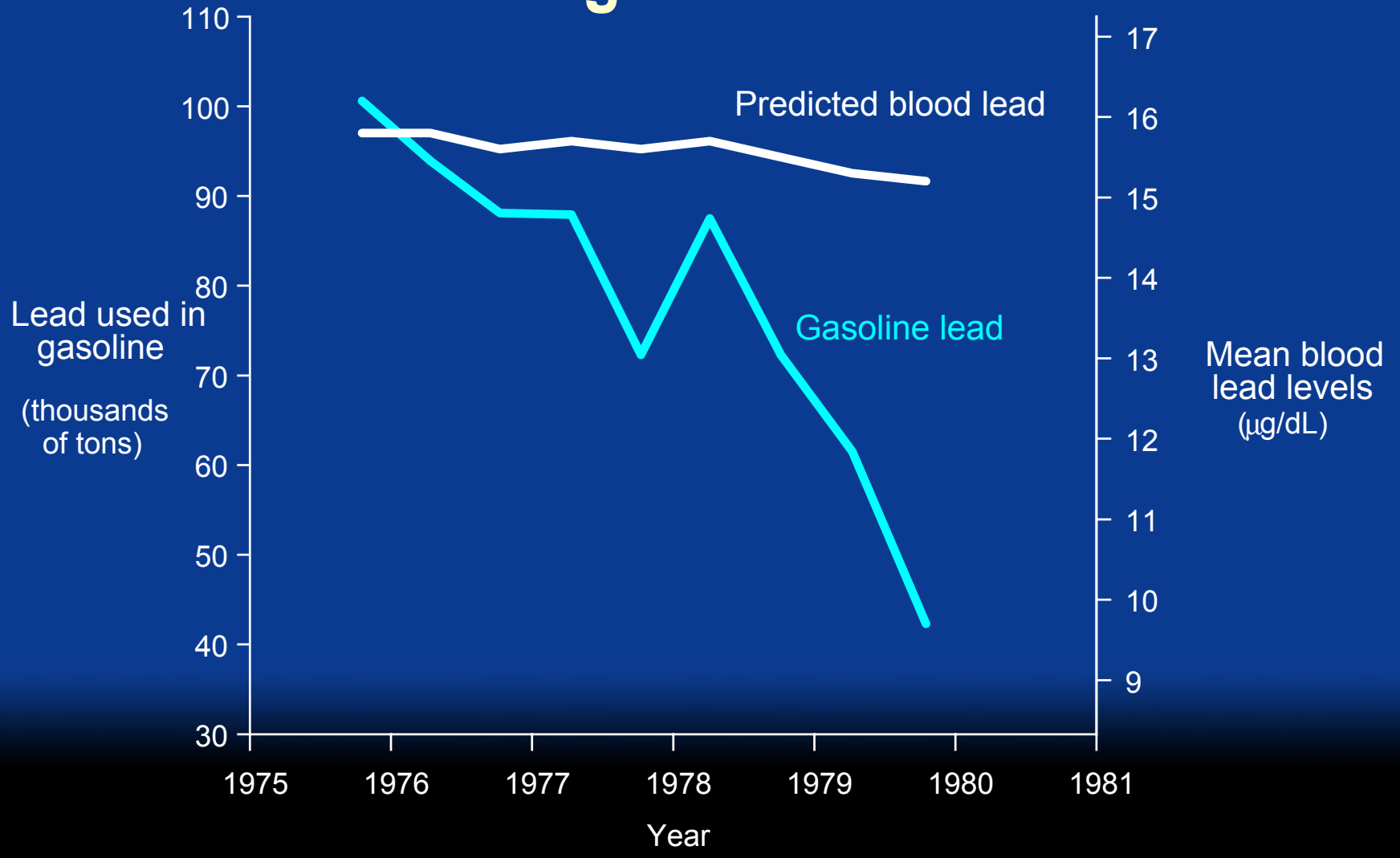
Blood lead levels (BLLs)

1 year of age and greater

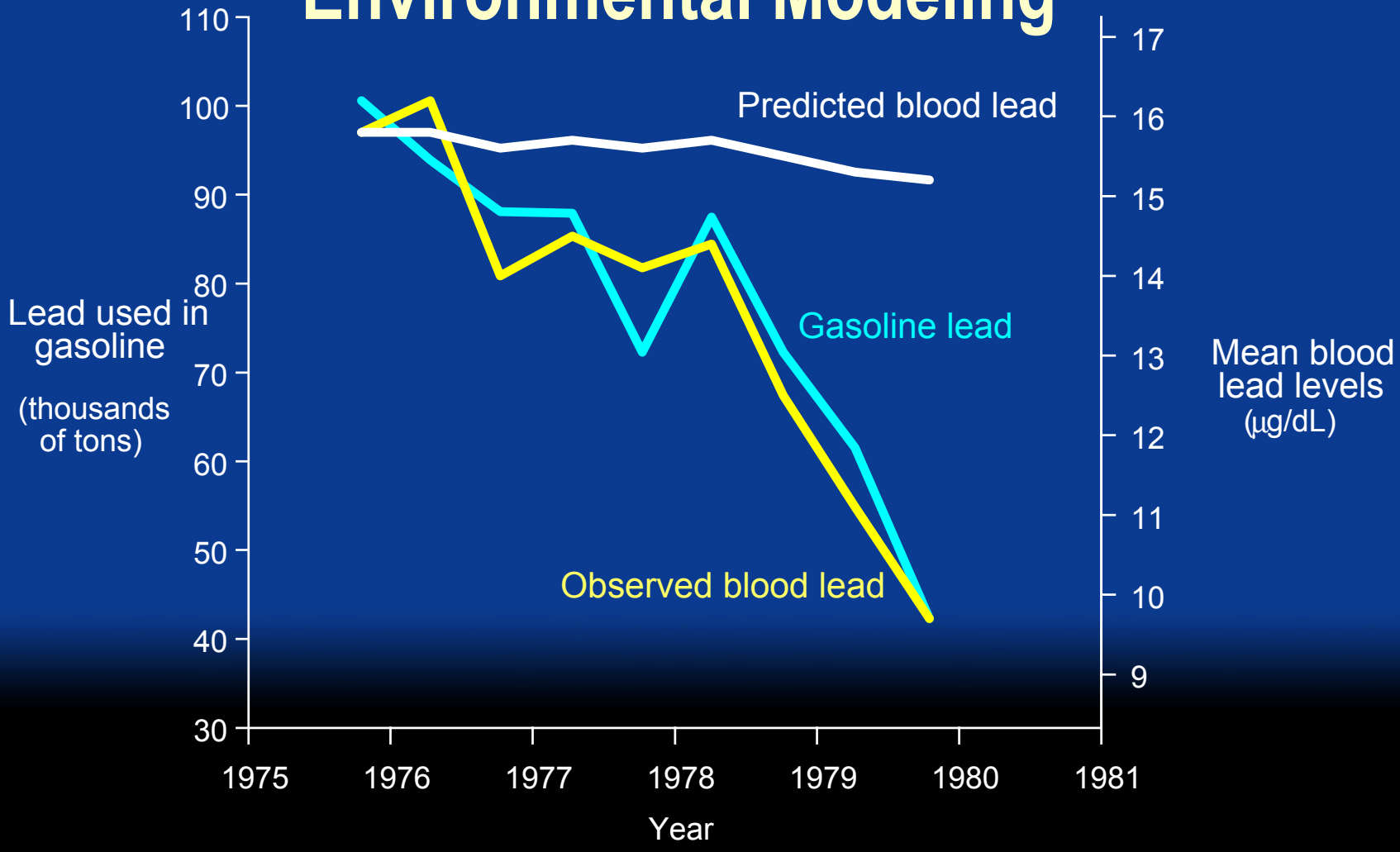
Lead Used in Gasoline Declined from 1976 Through 1980



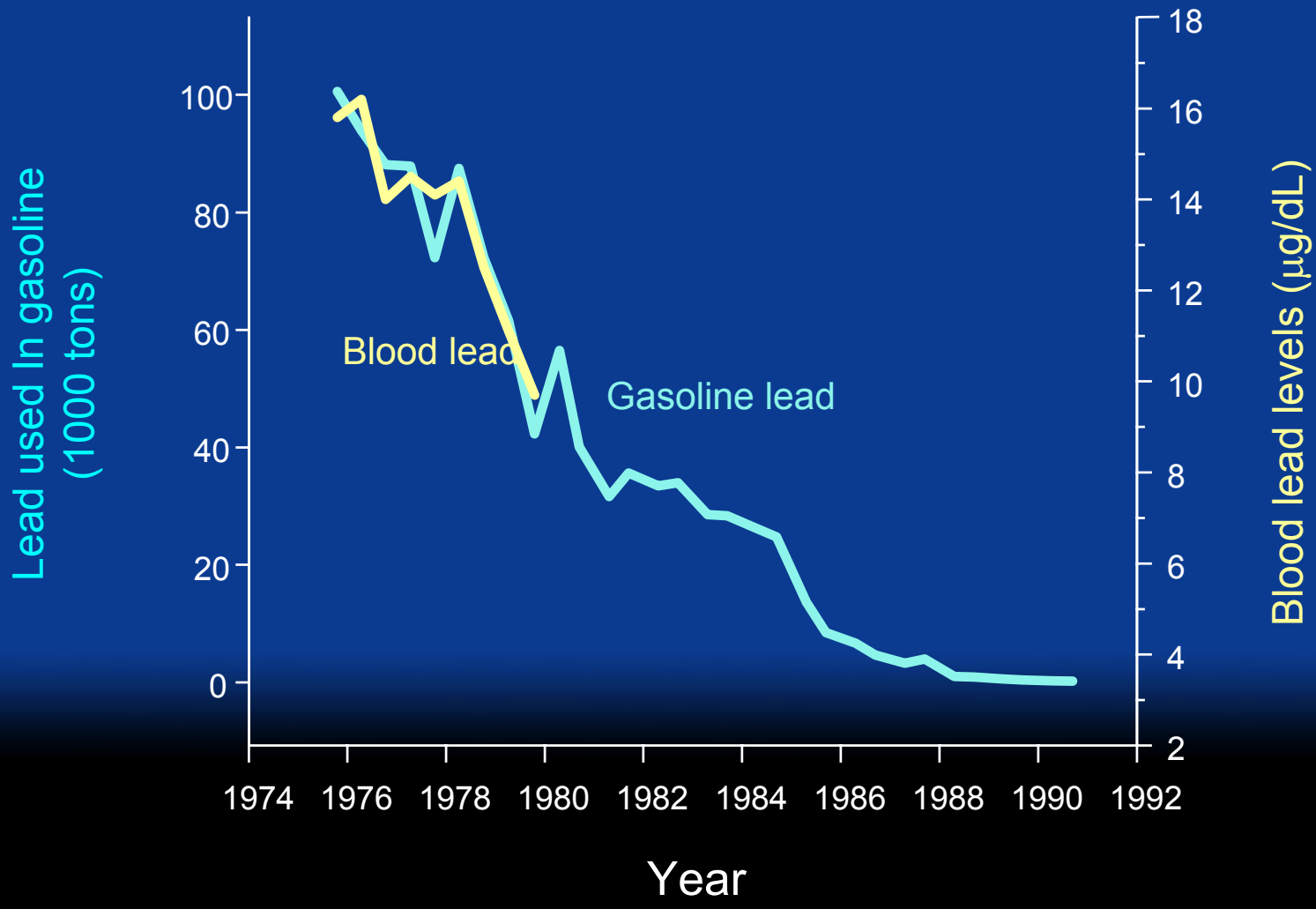
Predicted Blood Lead Changes with Decreasing Gasoline Lead



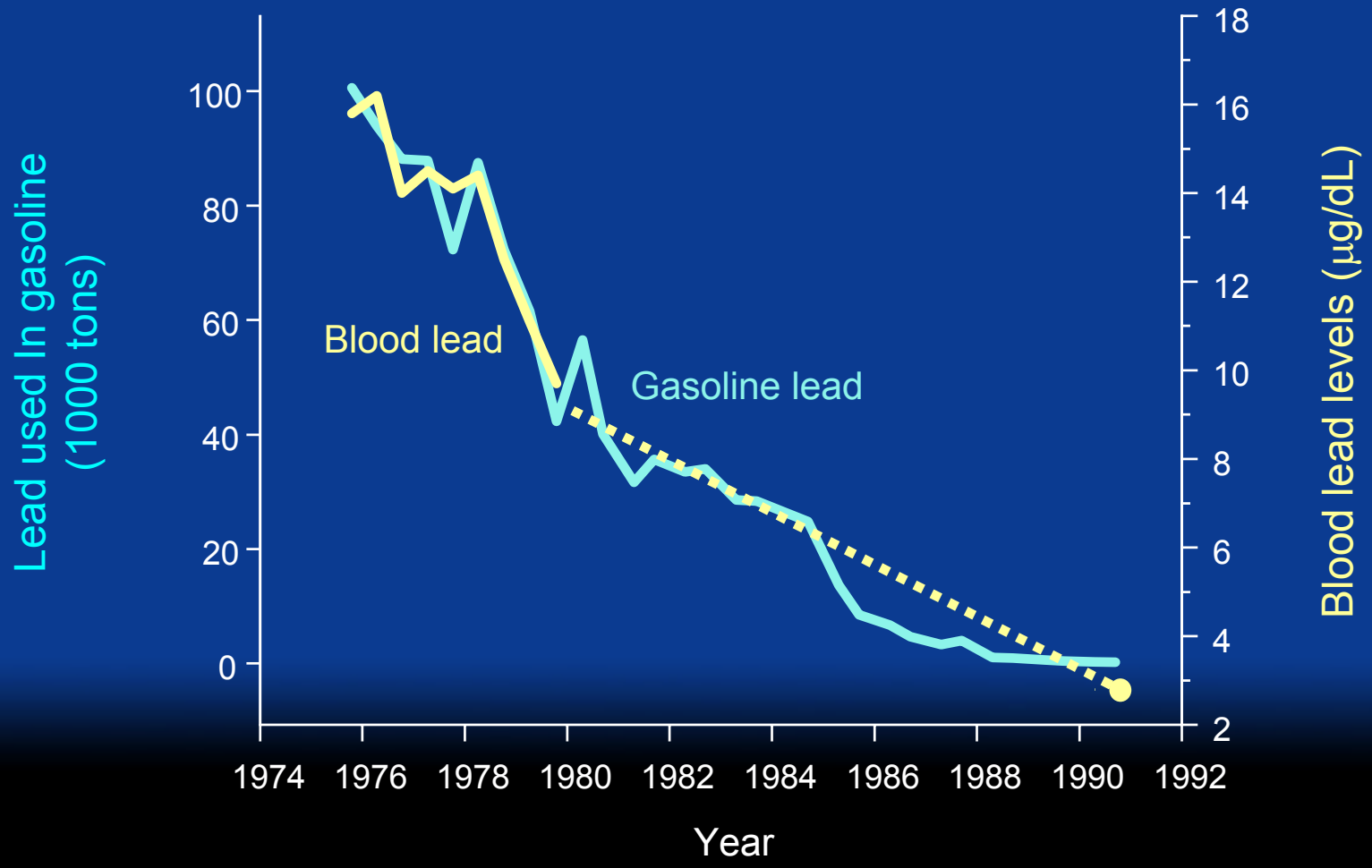
NHANES II Blood Lead Measurements Found A Substantial Decline in Blood Lead Levels, 10 Times More Than Predicted from Environmental Modeling



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

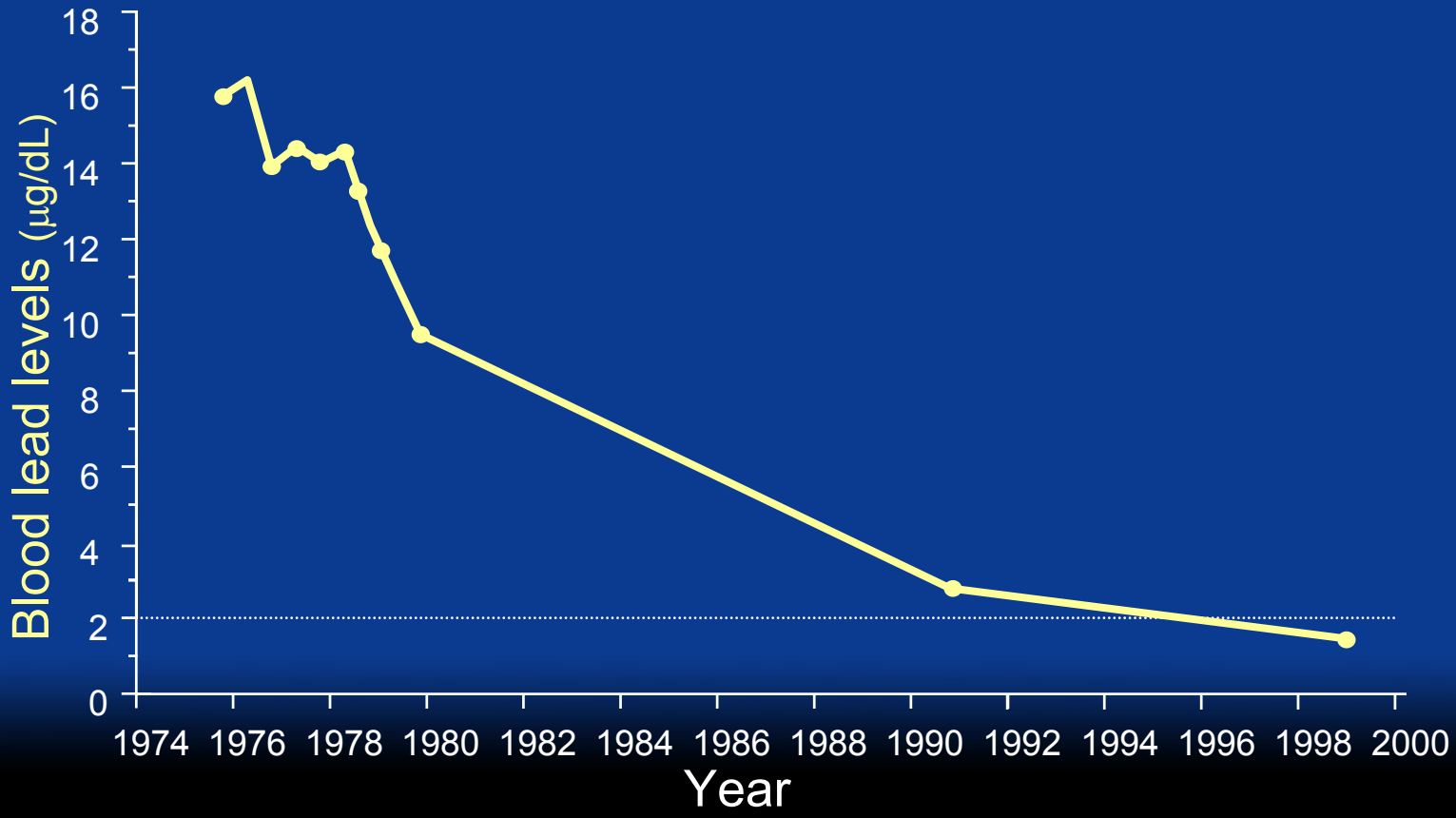


NHANES III (1988-1994) Showed Blood Lead Levels Continued to Decrease as Gasoline Levels Declined



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 μg/dL
  - 4.4% had BLLs ≥ 10 μg/dL

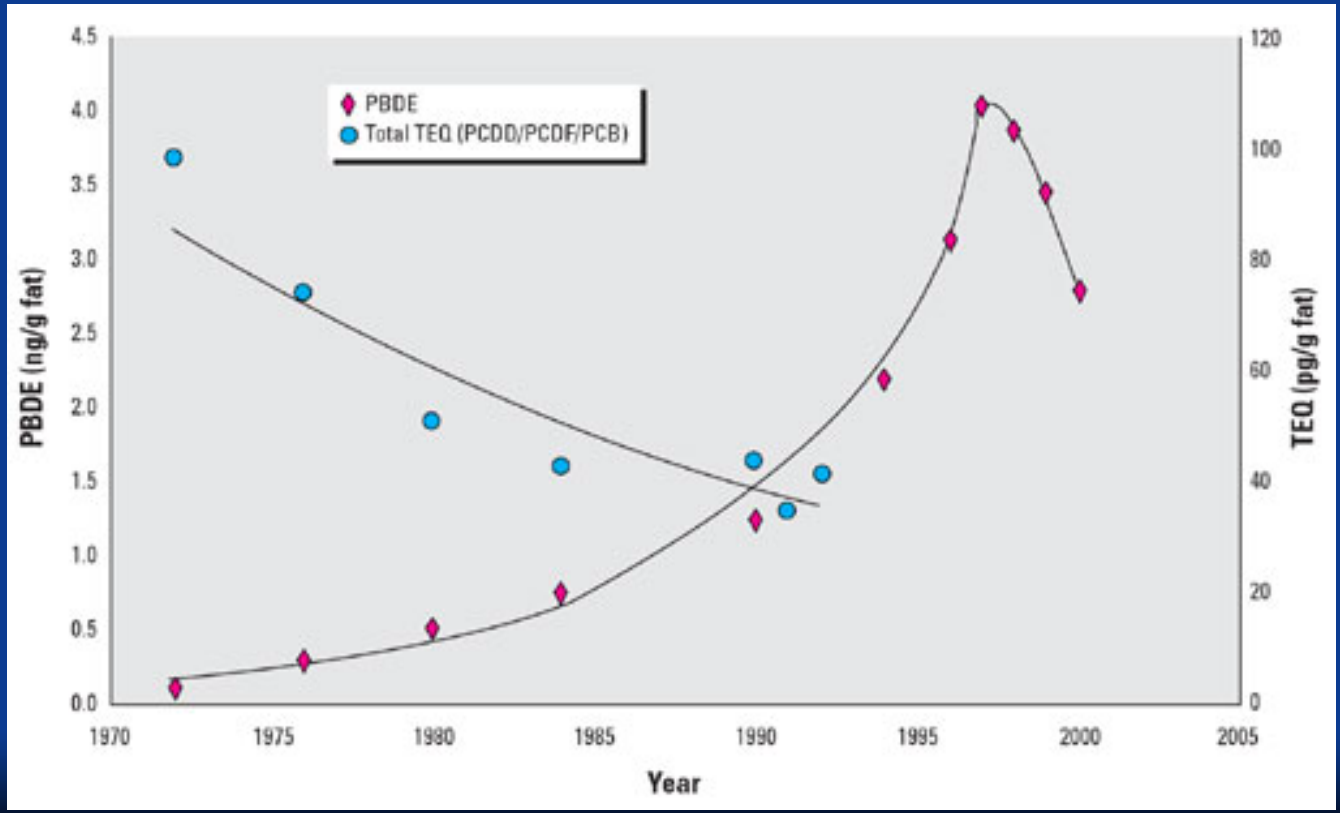
- NHANES 1999-2000
  - Geometric mean BLL 2.23 μg/dL
  - 2.2% had BLLs ≥ 10 μg/dL
  - Higher prevalence of BLLs in U.S. children occur in urban settings, lower SES, immigrants and refugees

(Geltman et al., 2001)

Geometric Mean BLLs

- Age groups (relative order of decreasing concentrations):
  1-5 years > 6-11 years > 20+ years > 12-19 years
- Gender: Males > Females
- Race/ethnicity: Non-Hispanic Black ~ Mexican American > Non-Hispanic White

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

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

Organophosphate Pesticides

- 8% total pesticide use in US
- About 50% of total insecticide treated areas in US
- 65% of insecticides applied in agriculture

Food Quality Protection Act of 1996

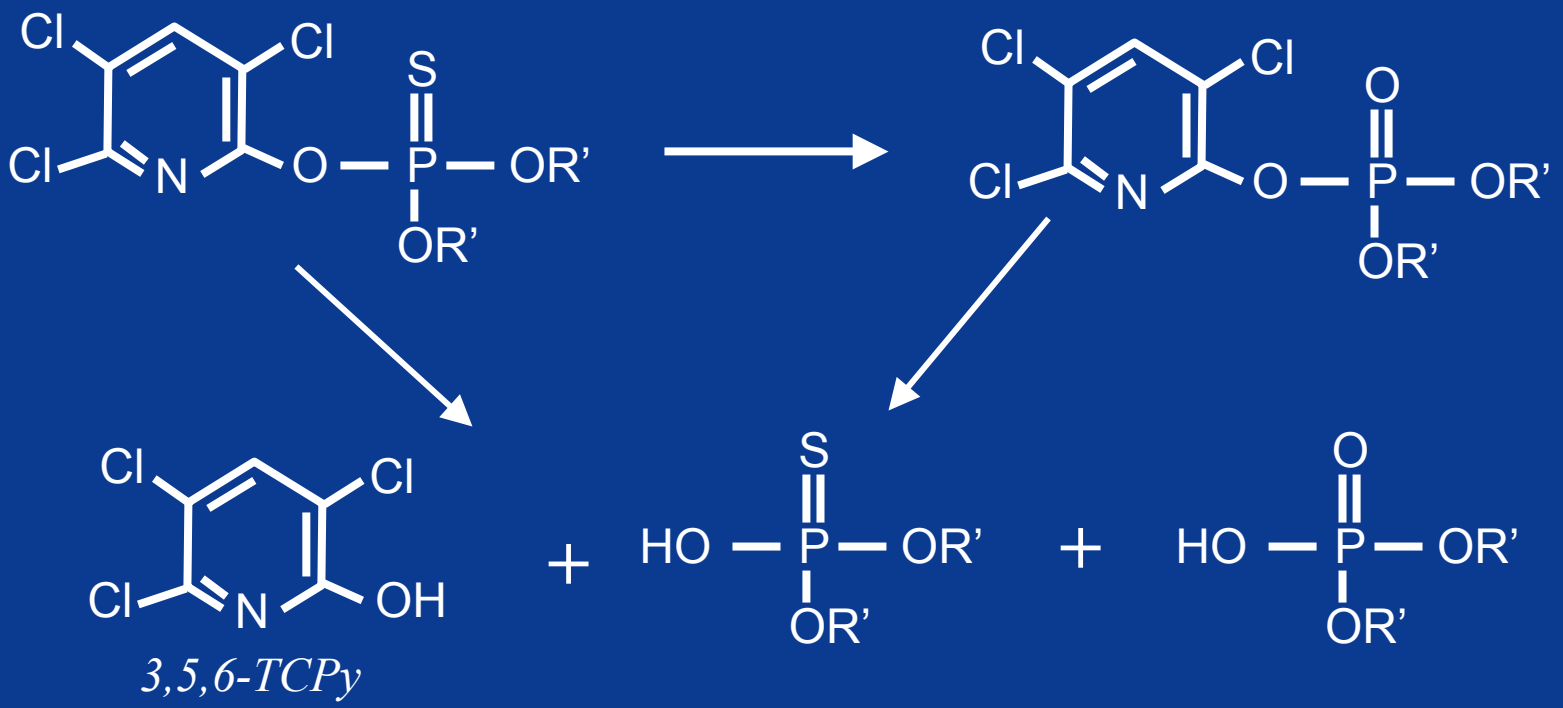
- EPA mandate to implement
- Exposure risk component with focus on children
- Aggregate and cumulative exposures
  - Aggregate – multiple route exposures
  - Cumulative – 2 or more chemicals with same mechanism of action
- Organophosphate insecticides
  - Safety factor (≤ 10 fold) for children
  - Most reevaluated
  - Chlorpyrifos, diazinon use restricted
- Evaluate efficacy of implementation with NHANES III, NHANES 99+, and beyond

Organophosphate (OP) Pesticides

Metabolites in Urine

6+ years

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



3,5,6-TCPy is "specific" metabolite

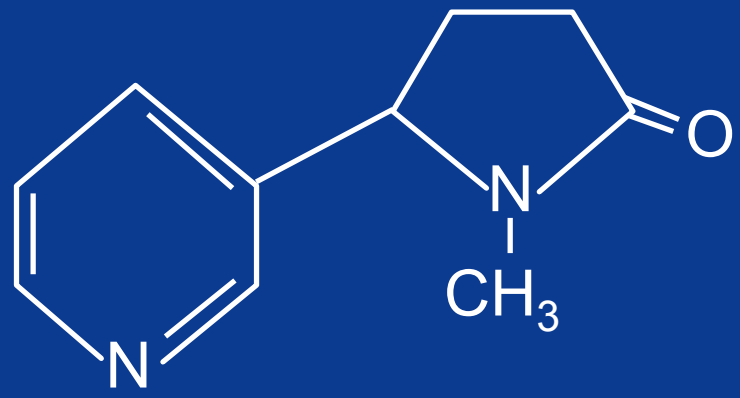
Dialkyl phosphates are "nonspecific" metabolites

OP Pesticide - Metabolism

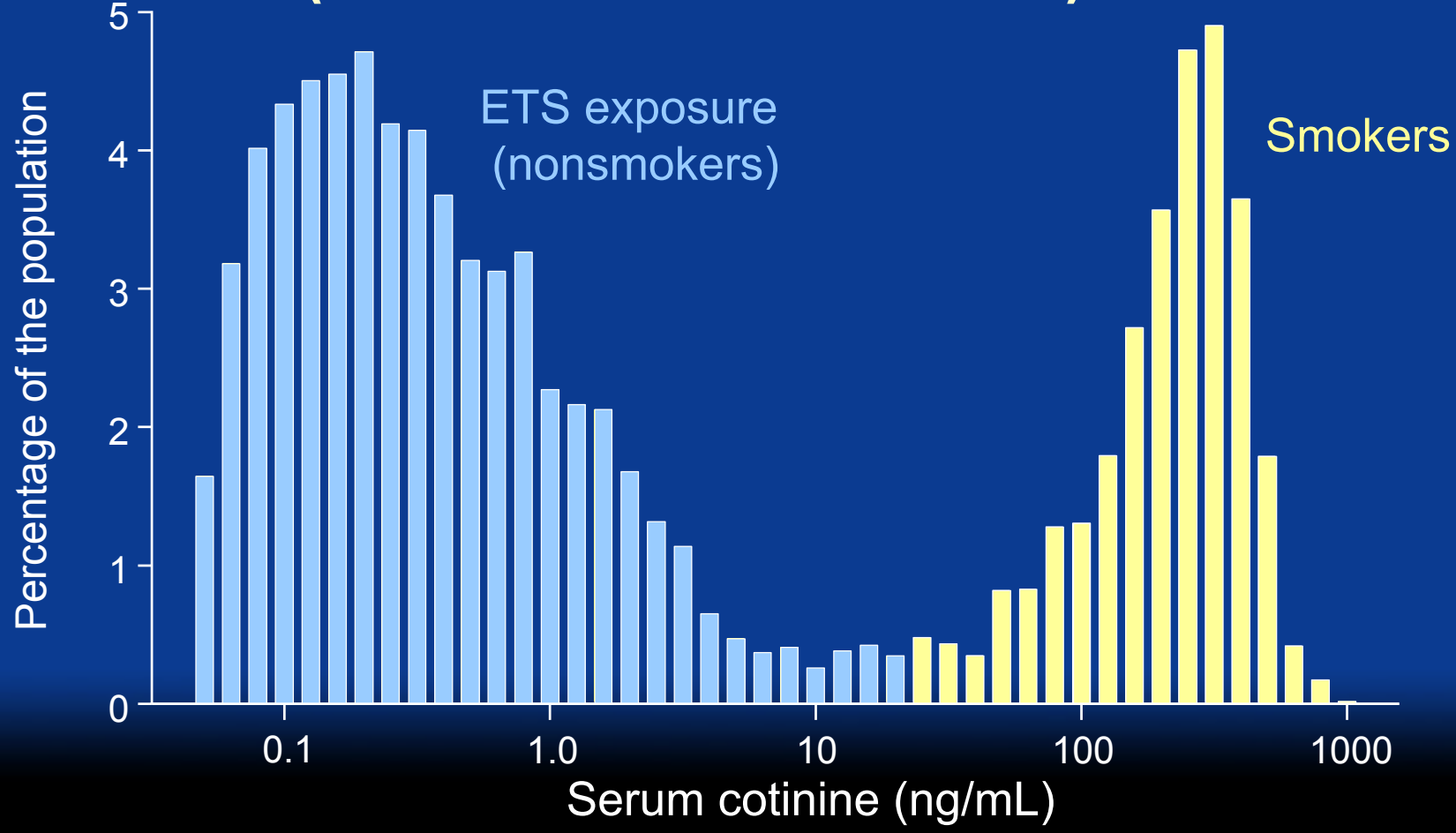
- Of 39 EPA-registered OP pesticides, 28 metabolize to 6 dialkyl phosphates; DMP, DMTP, DMDTP, DEP, DETP, DEDTP
- These 6 dialkyl phosphates are nonspecific for identifying parent OP
- Useful for tracking reduction of OP pesticide use
- Children had significantly higher concentrations than adults
- Little differences observed among race/ethnicity, or gender

Cotinine

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



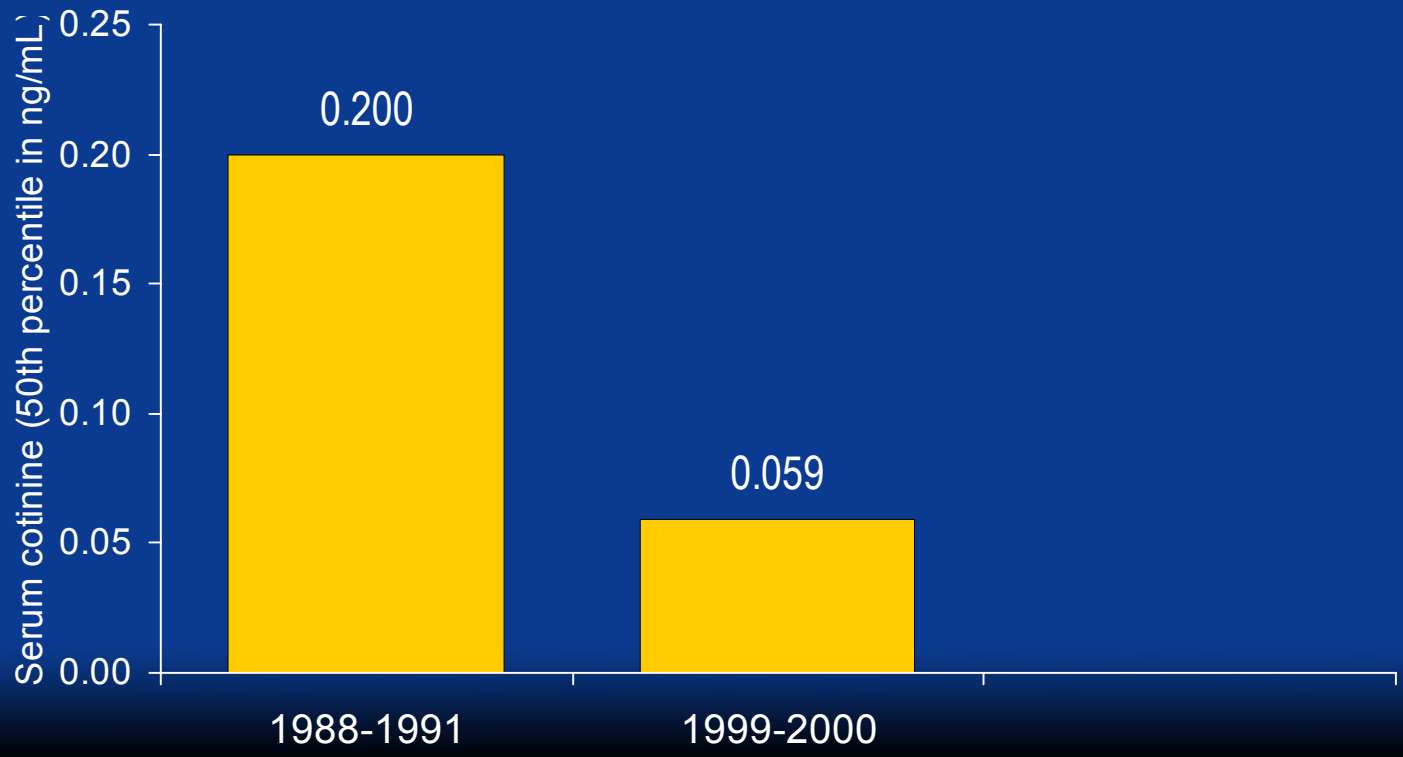
Exposure of the U.S. Population to Tobacco Smoke: Serum Cotinine Levels (NHANES III, 1988-1991)



Second Report Results

- Decrease in ETS 1988-91 to 1999-2000
  - Measured as serum cotinine
  - Children: 58% decreased
  - Adolescents: 55% decreased
  - Adults: 75% decreased

Decline in Exposure of Nonsmokers in the U.S. Population to Environmental Tobacco Smoke

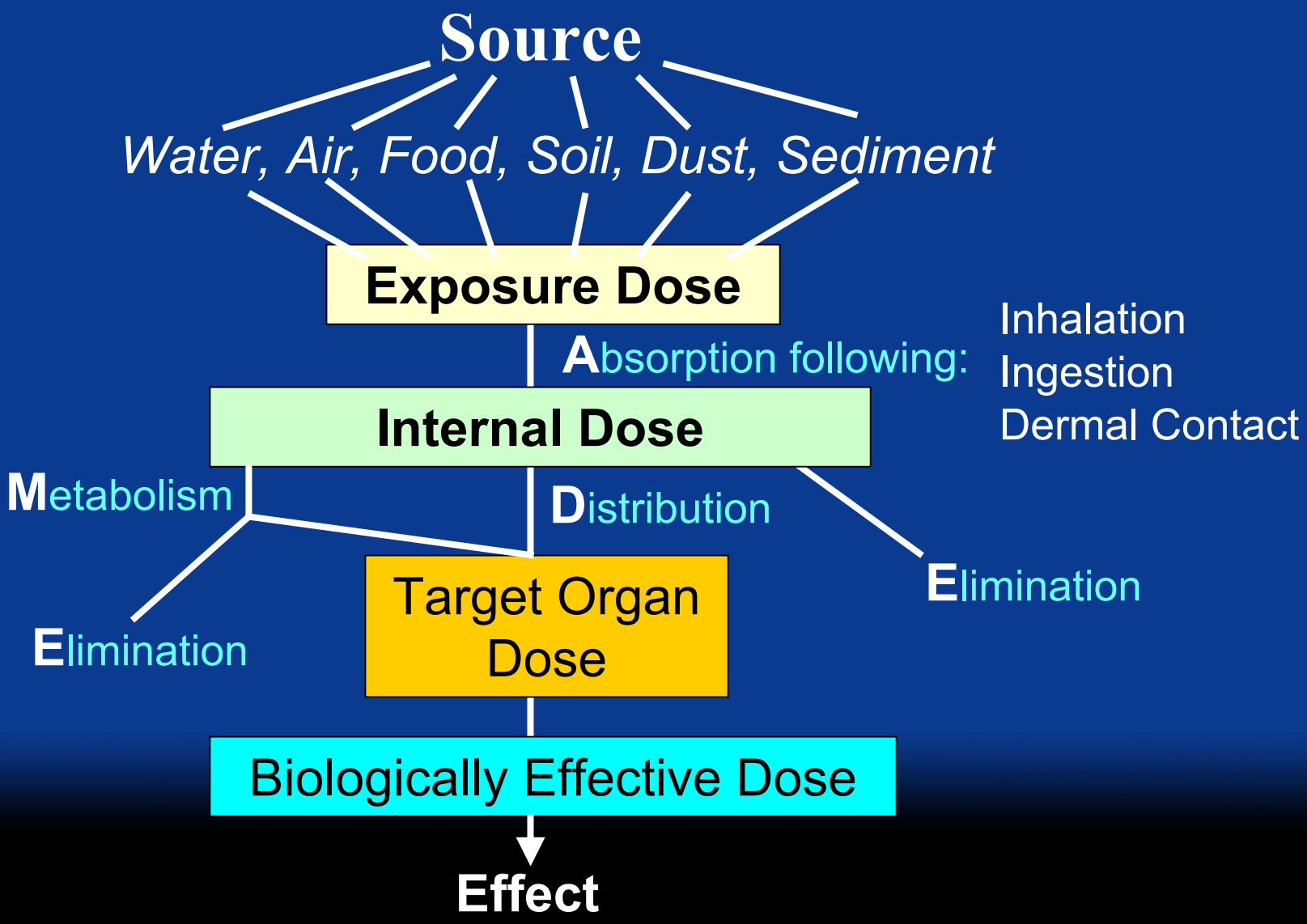


Additional Chemicals in Future National Reports

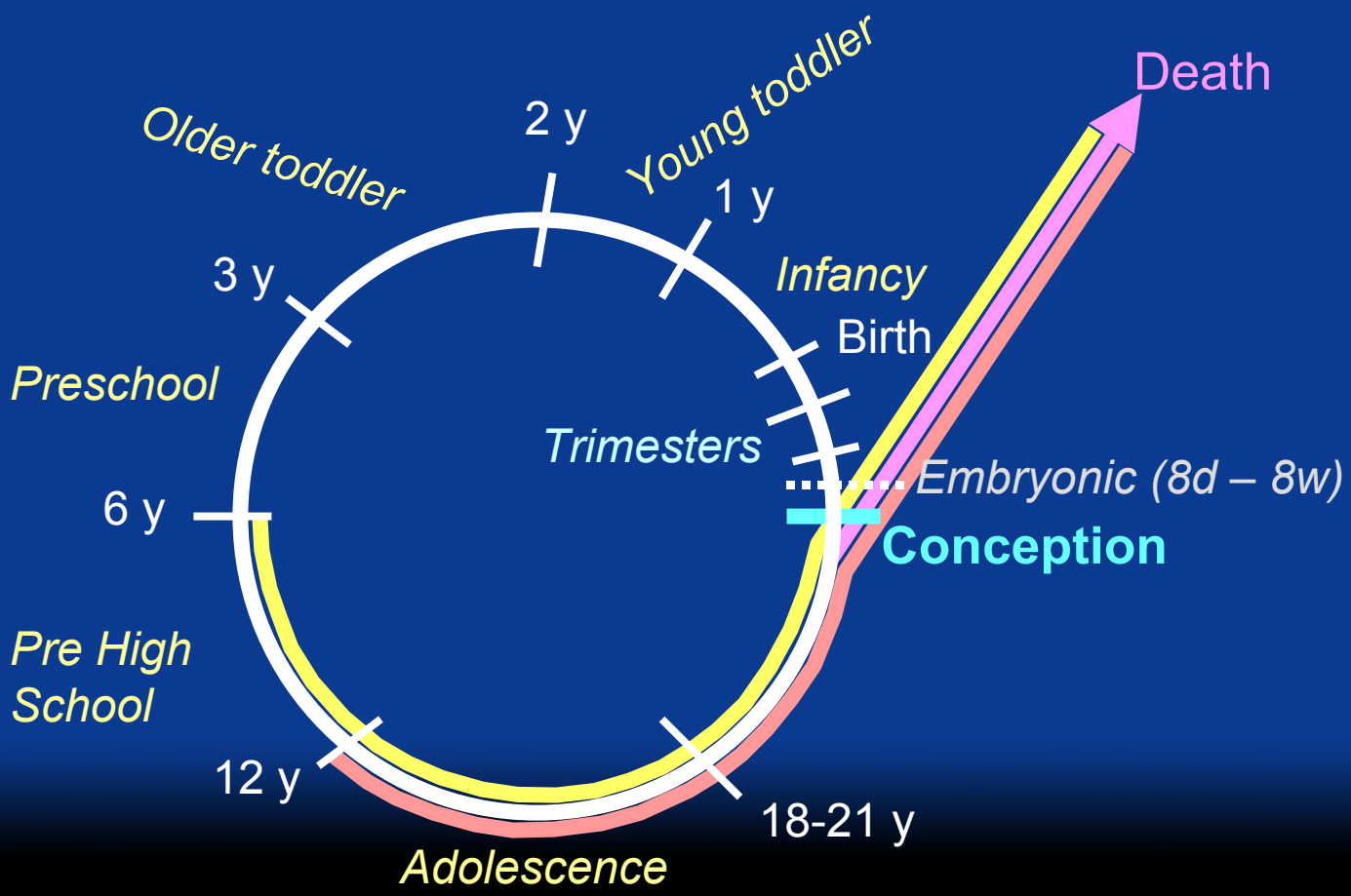
Brominated flame retardants
Perfluorinated chemicals (PFOS/PFOA)
Bisphenol A
Pyrethroids
Alkyl phenols

Additional phthalate metabolites
Additional specific OP pesticide metabolites
Additional organochlorine chemicals
Arsenic (speciated)
Acrylamide
30+ Volatile Organic Chemicals

Exposure Pathway



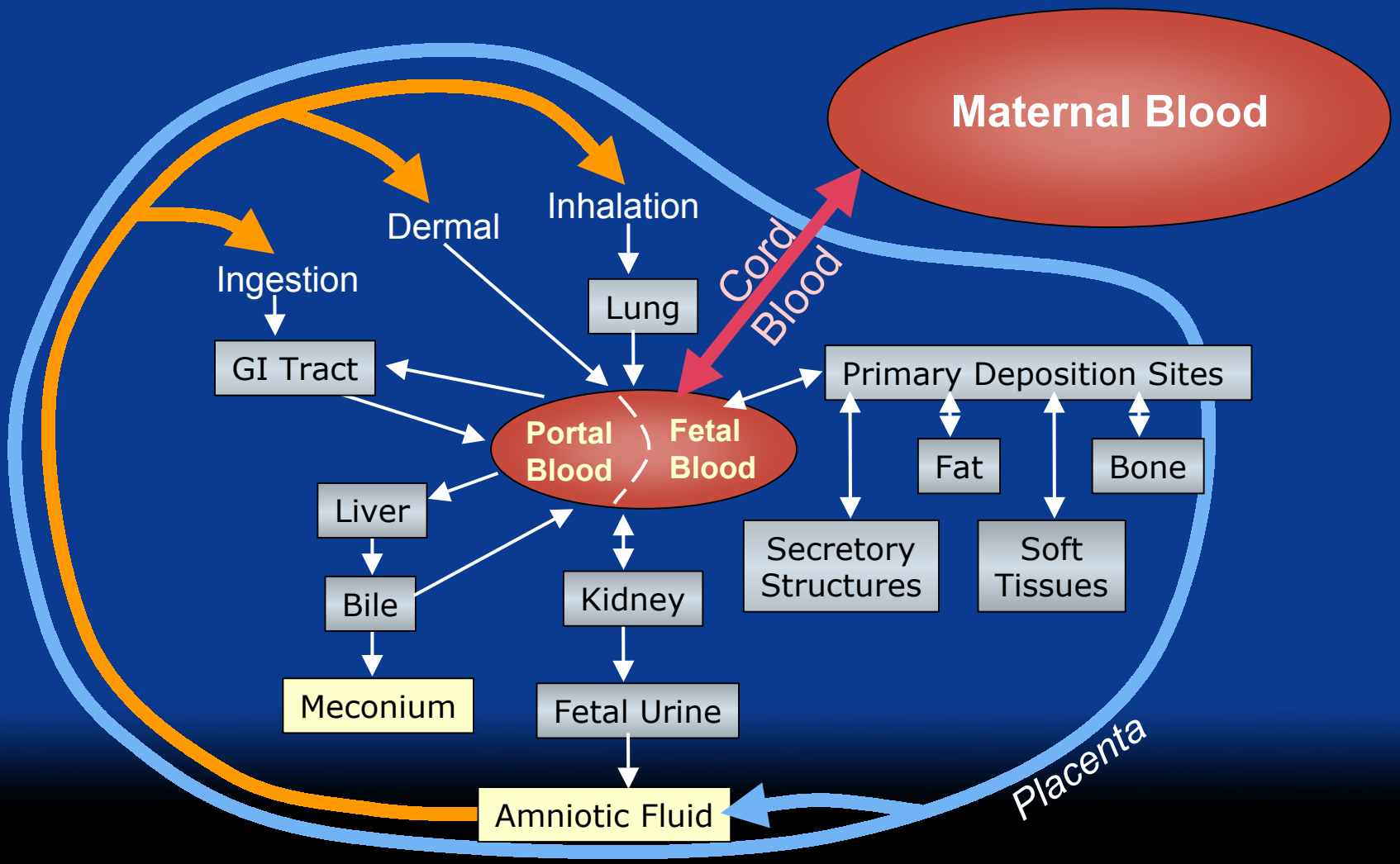
Life Stages of Children



NHANES Biomonitoring: Limitations of and Needs for Supplementing

- Age Range
  - Limitation: Younger ages not sampled
  - Need: Special Studies
    - EPA/NIEHS Children's Centers/other children's studies
    - Validation of alternative matrices

Biomonitoring: Fetal Period/Fetal Environment



NHANES Biomonitoring: Limitations of and Needs for Supplementing

- Special Studies
  - Upper 5% (Hot Spots)- look for association with outcomes
  - Known health effects- exposure assessment (Case/Control)
  - Characterization of exposure changes over time within an individual (Longitudinal)
  - Environmental degradation studies for selected chemicals; e.g., OP pesticides

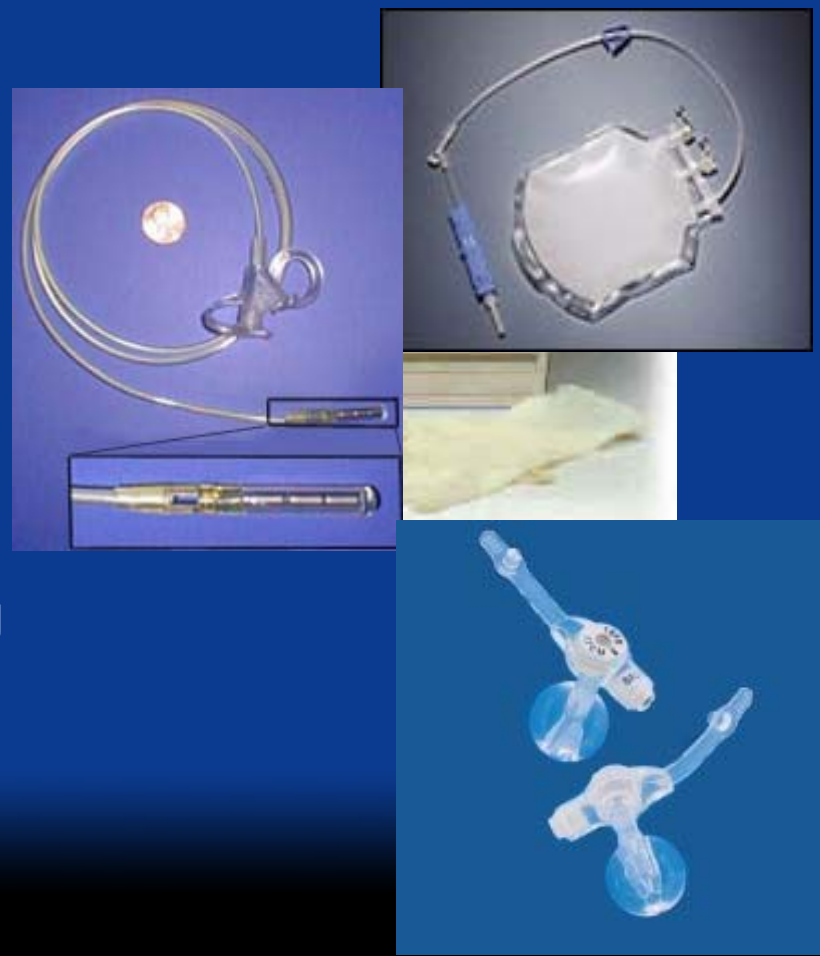
Exposure to DEHP in Critically Ill Neonates

- Collaborative study with UMDNJ/RWJMS
- Measure 3 urinary DEHP metabolites
- 6 premature children
  - 4 females
  - 24.9 ± 1.6 weeks
  - 665.5 ± 166.5 grams
  - 59 urine samples
    - 9 ± 6 samples/child

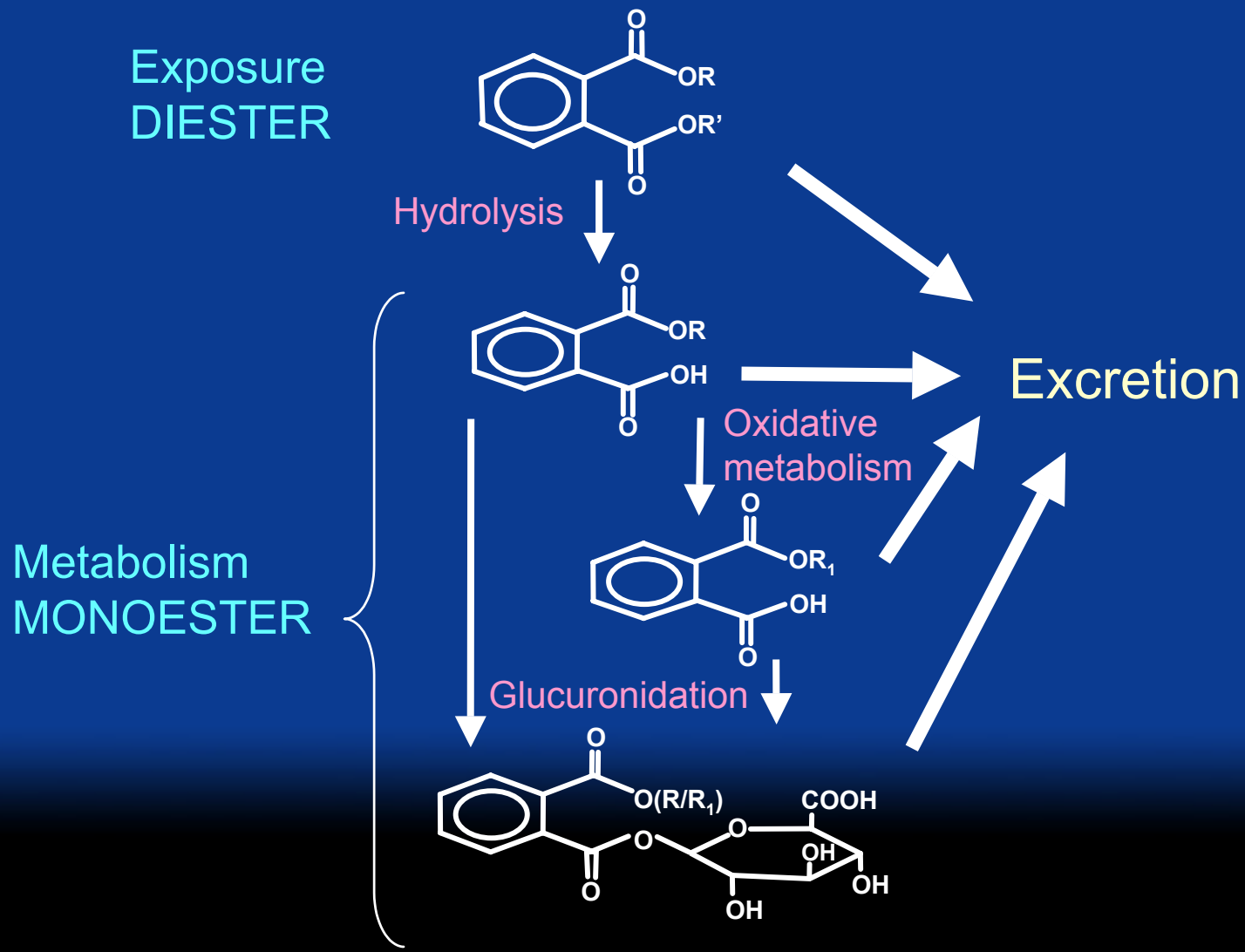
- Eligibility criteria
  - To be on intravenous infusion for at least a couple of weeks
  - Expected to survive

DEHP-plasticized Items in the NICU

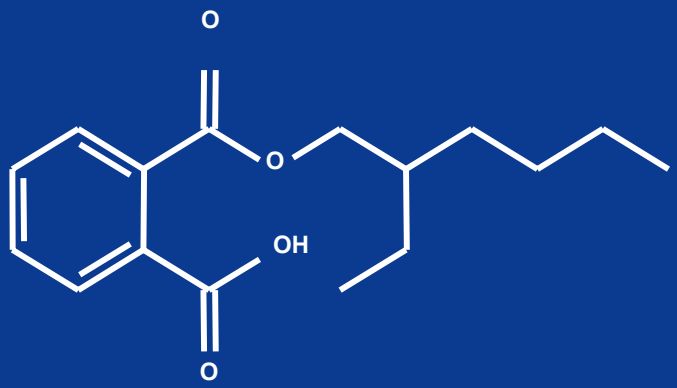
- Feeding-related
  - Nasogastric tubes
- Respiratory therapy
  - Ventilator tubing
- Intravenous therapy
  - IV bags and tubing
  - Blood bags and tubing
- Miscellaneous
  - Examination gloves



Metabolism of Phthalates



DEHP Metabolites



mEHP

mEOHP

mEHHP

DEHP Metabolites in Neonates