

Chemical Exposure and Chronic Disease

Sarah Janssen, MD, PhD, MPH

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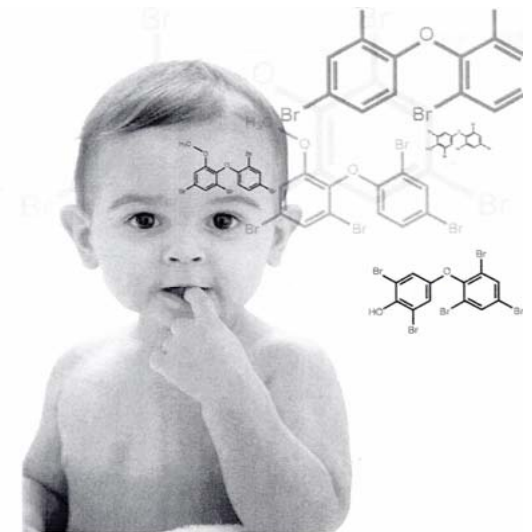
USA

sjanssen@nrdc.org

IPEN side event at IFCS, Budapest, September 25, 2006

Background

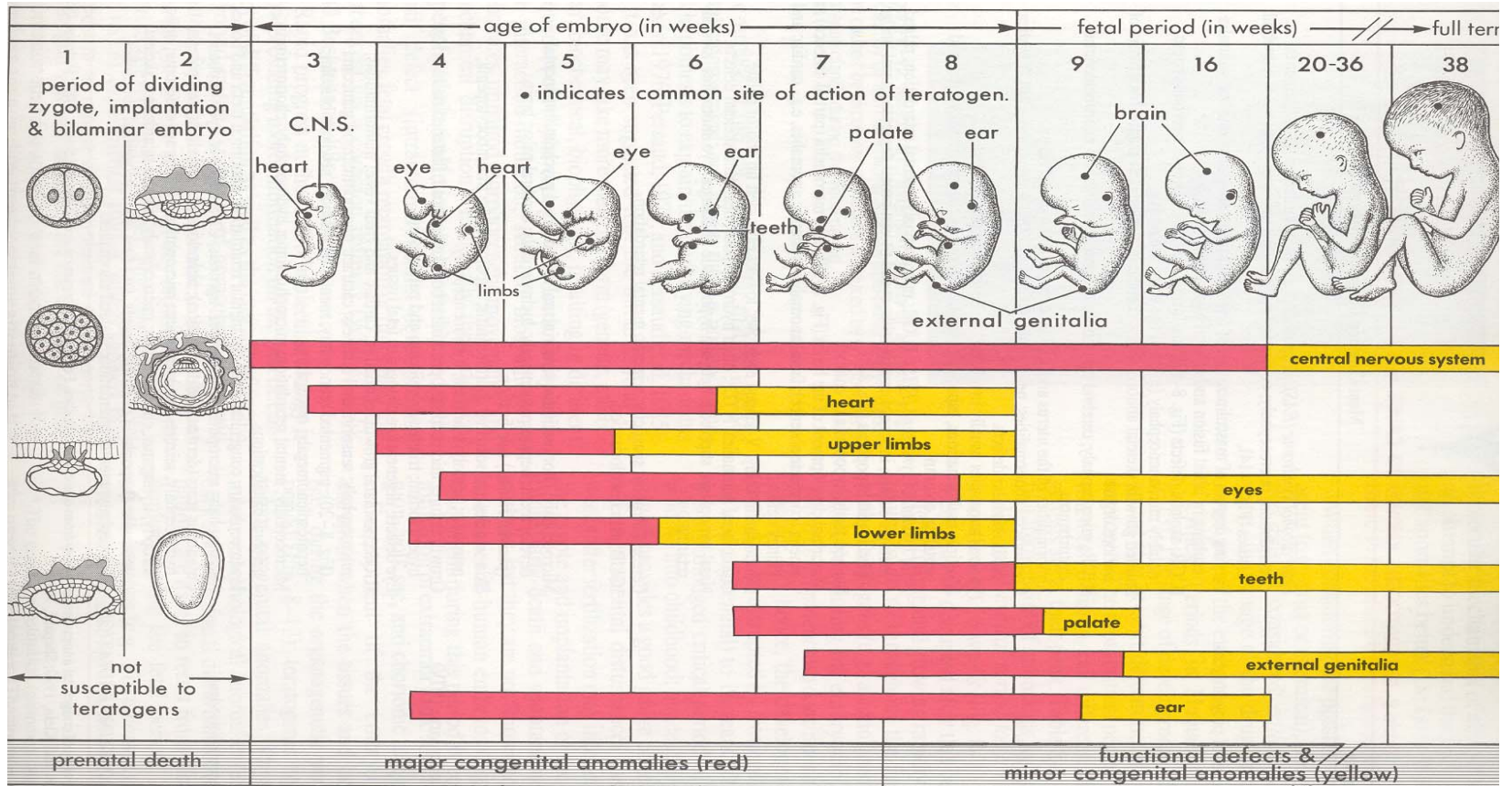
- Many chemicals have been associated with human disease
- Health effects can occur from both occupational and environmental exposures
- We are exposed to multiple chemicals through multiple routes throughout our lives



Main points

- Timing and routes of exposure - as critical as dose and type of chemical exposure
- Fetal origins of disease
- Effects can be subtle and not easily recognized
- Threshold of safety?

Embryonic Development & Vulnerability



Children are More Vulnerable to All Toxins

- Immature brain, blood/brain barrier;
- Eat, breathe & drink more per kg;
- GI & skin 2x surface area v. adult;
- Outside more & closer to ground;
- Hand/mouth behaviors;
- Mouth breathers;
- Lower enzyme levels.



Lead

A Well-Recognized Neurotoxicant



- Old paint & water pipes
- Home renovation (in dust)
- Gasoline
- Industrial/workplace emissions
- Electronics manufacturing and recycling
- Batteries, pigments, stabilizers
- Bullets and fishing weights
- Costume jewelry & pottery
- Folk remedies
- Vinyl and non-glossy mini-blinds

Effects of Lead on Children's Cognitive and Behavioral Traits

Increases

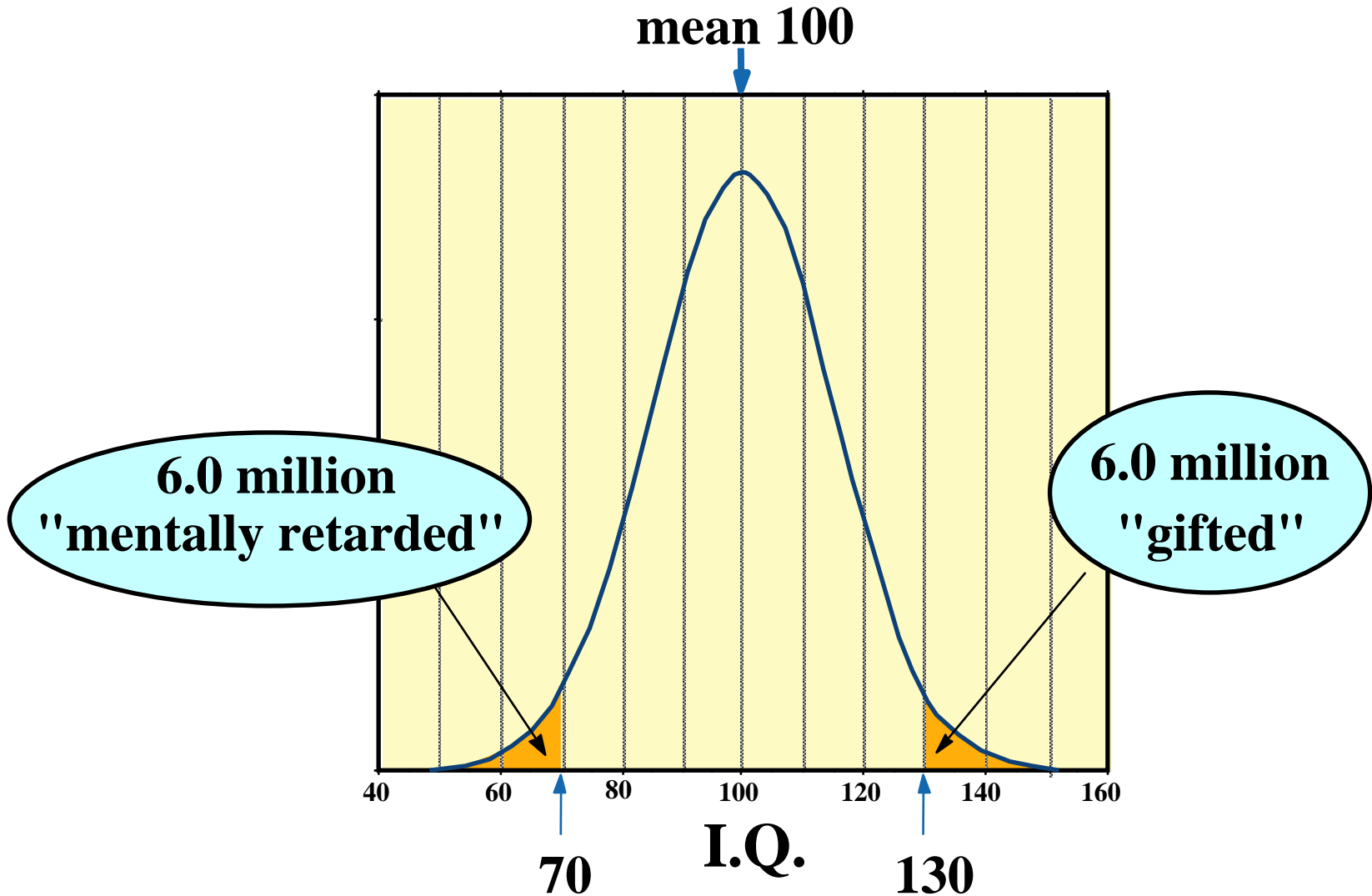
- hyperactivity
- impulsivity
- distractibility
- difficulty following instructions
- conduct problems
- aggressiveness
- antisocial behavior

Decreases

- attention
- social skills
- reading, math skills
- spelling
- pattern recognition
- word recognition
- problem solving skills
- fine motor
- visual motor

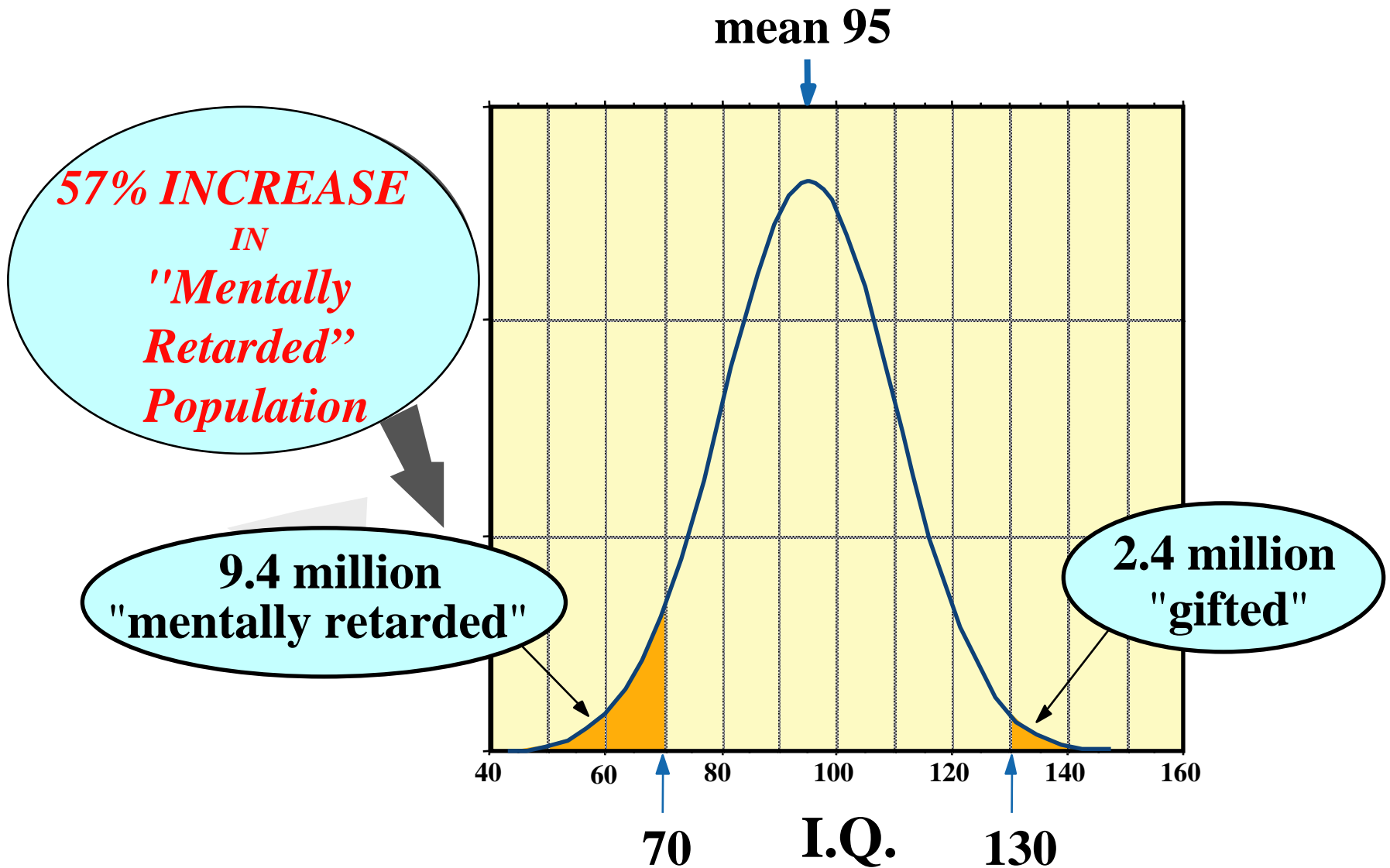
The Significance of Small Effects:

EFFECTS OF A SMALL SHIFT IN IQ DISTRIBUTION IN A POPULATION OF 260 MILLION

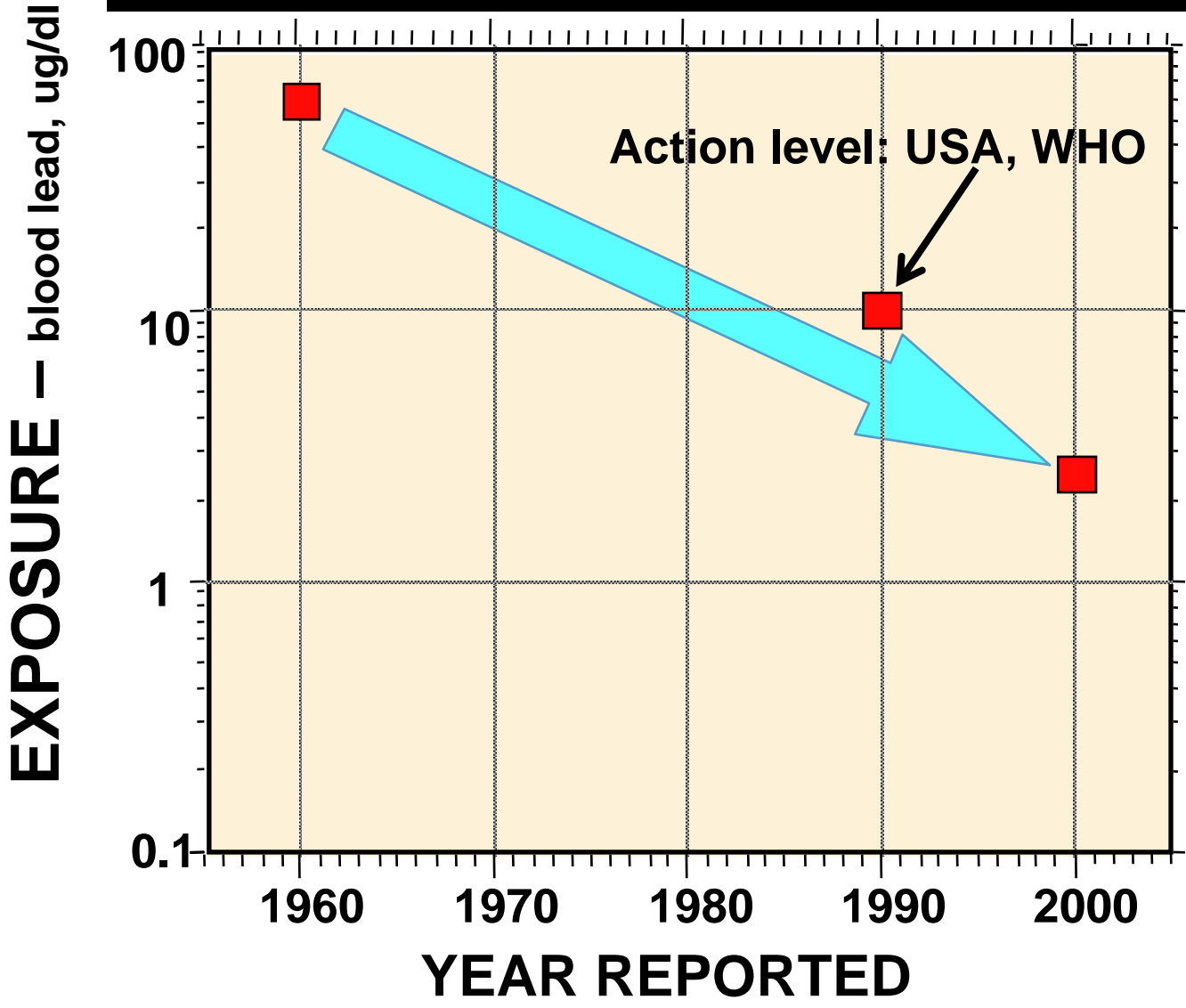


5 Point Decrease in Mean IQ

just one IQ point drop ~ 2.4% reduction in lifetime earnings



DECLINING THRESHOLD OF HARM - LEAD



Note: Exposures expressed in micrograms/deciliter (blood lead)

Other Health Effects of Lead Exposure

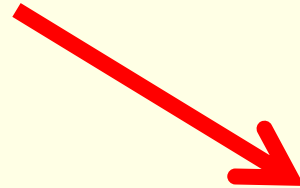
- Cognitive Decline and Dementia
- Hypertension
- Atherosclerosis
- Peripheral neuropathy
- Behavioral changes
- Reduced sperm count and libido
- Chronic renal disease, nephritis
- Miscarriages
- Brain cancer

Mercury – a Persistent Problem



Power plants
Incinerators
Boilers
Chlor-alkali industry

Cement kilns
Mining
Natural off-gassing



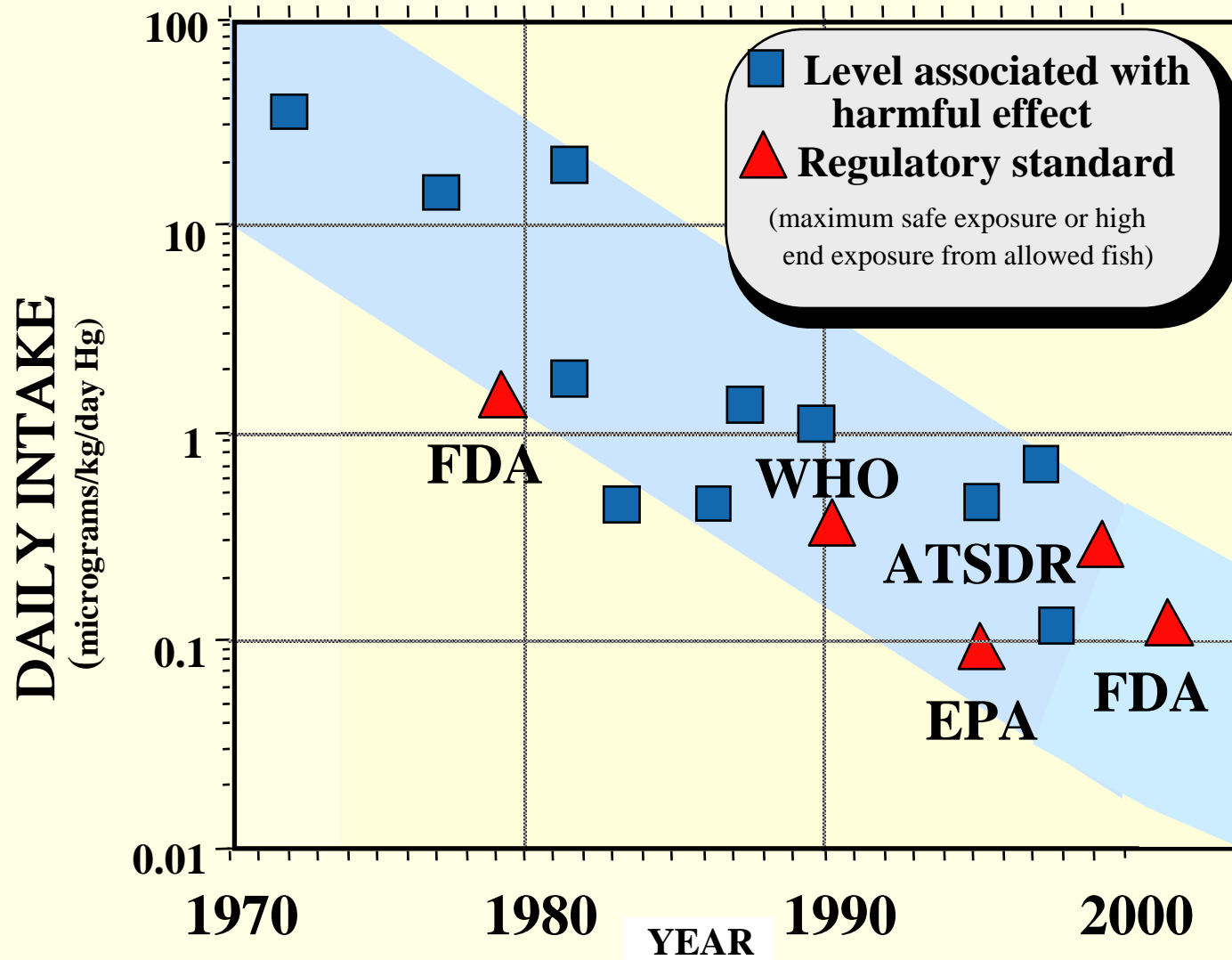
Methylation in Sediments
Bioaccumulation in wildlife
fish, and humans.



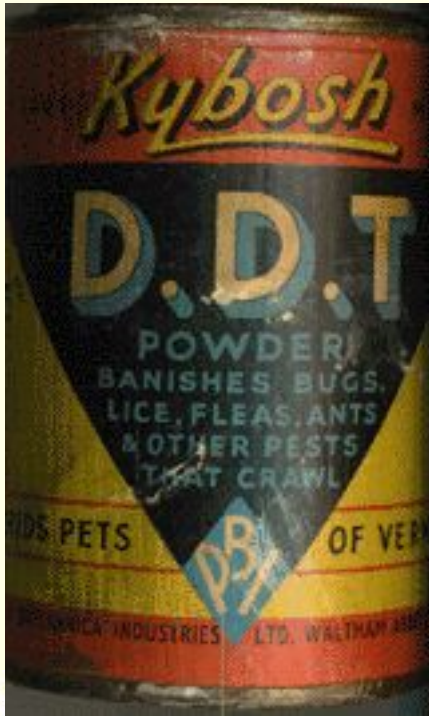
Organic Mercury: Prenatal Exposure Effects

- Neurological deficits/Mental retardation
- Seizures
- Cerebral palsy
- Disturbances of vision, hearing, sensation
- Abnormal gait
- Abnormal speech
- Disturbances of swallowing and sucking
- Abnormal reflexes

Mercury: Declining Threshold of Harm



Pesticides



10 Lb. Dursban[®] Lawn & Garden Insect Control

7.99
10 Lb.

20 Lb. Dursban[®] Lawn & Garden Insect Control

15.99
20 Lb.

**• The Law Is Changing!
Last Day To Buy Dursban[®]
Will Be Here Soon!**

NOTICE
If Dursban[®] is sold out when you receive this ad, Scotty's will sell you the replacement, Diazinon...45765, for the same sale price.

**Controls Surface & Foliage Pests, Soil Insects,
Helps Control Home Invading Pests
& Vegetable Garden Insects**

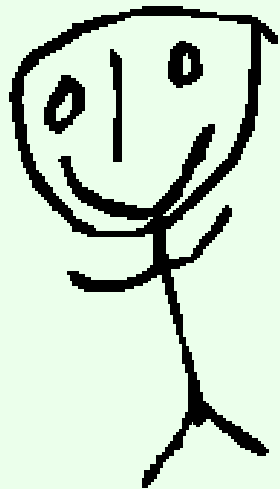
Controls: Fleas, ticks, white grubs, mole crickets, ants, sod webworms, lawn bugs, armyworms, grasshoppers, crickets, earwigs, sowbugs, silverfish, spiders, wireworms, cutworms, root maggots, billbugs, chiggers

CAUTION See label for directions.

THESE HOT BUYS WILL END FRIDAY, MAY 11TH

Neurotoxicity of Pesticides in Children

Foothills



54-Month-old
female



55-Month-old
female

Valley



54-Month-old
female



53-Month-old
female

Adult Neurotoxic Effects

- Occupational exposures to organophosphate or carbamate pesticides can result in:
 - permanent loss of short-term memory and psychomotor speed, and behavioral symptoms including anxiety, irritability and depression.

Reproductive and Developmental Toxicity

- 12 pesticides are listed by the State of California as known to cause birth defects or other reproductive harm.
- Workers exposed to pesticides have increased risks of miscarriage, infertility, and a variety of birth defects.
- Poor semen quality has also been associated with pesticide exposure

Endocrine Disruptor

- “An exogenous agent that interferes with the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis, reproduction, development, and /or behavior.”

U.S. EPA, February 1997

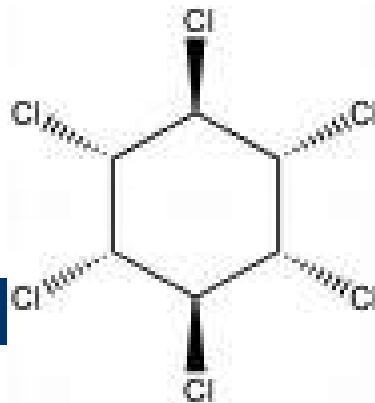
- Or in simpler terms:

“A substance which interferes with natural hormones.”

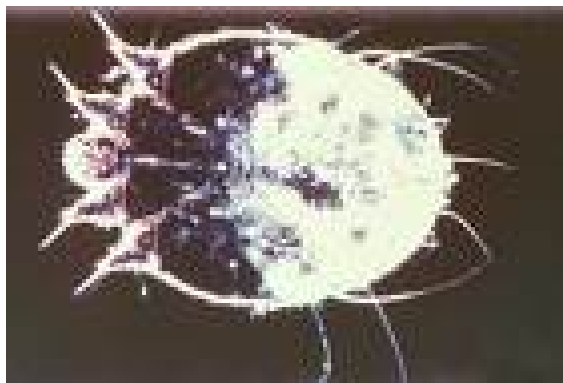
Endocrine Effects of pesticides

- Some mimic or block estrogen, others have been shown to block androgens or thyroid hormone.
- In animals effects include altered circulating hormone levels, hypospadias, nipple development in males, cryptorchidism, decreased semen quality, altered time to puberty, and abnormal behavior

Lindane



HCH



Life cycle concerns



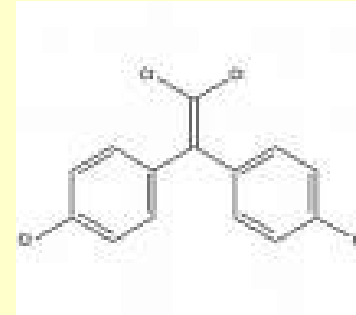
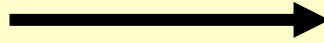
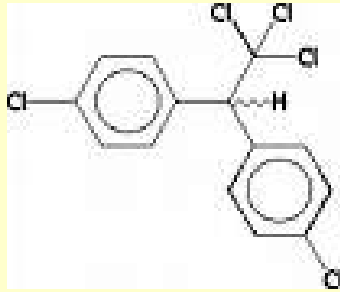
Photo courtesy of John Vijgen.

Lindane Toxicity

- Endocrine disruptor
- Neurotoxicity in children, elderly, immunocompromised
- Changes in circulating antibody levels
- Possible carcinogen

Not the most effective treatment for lice/scabies
- 17% killing rate

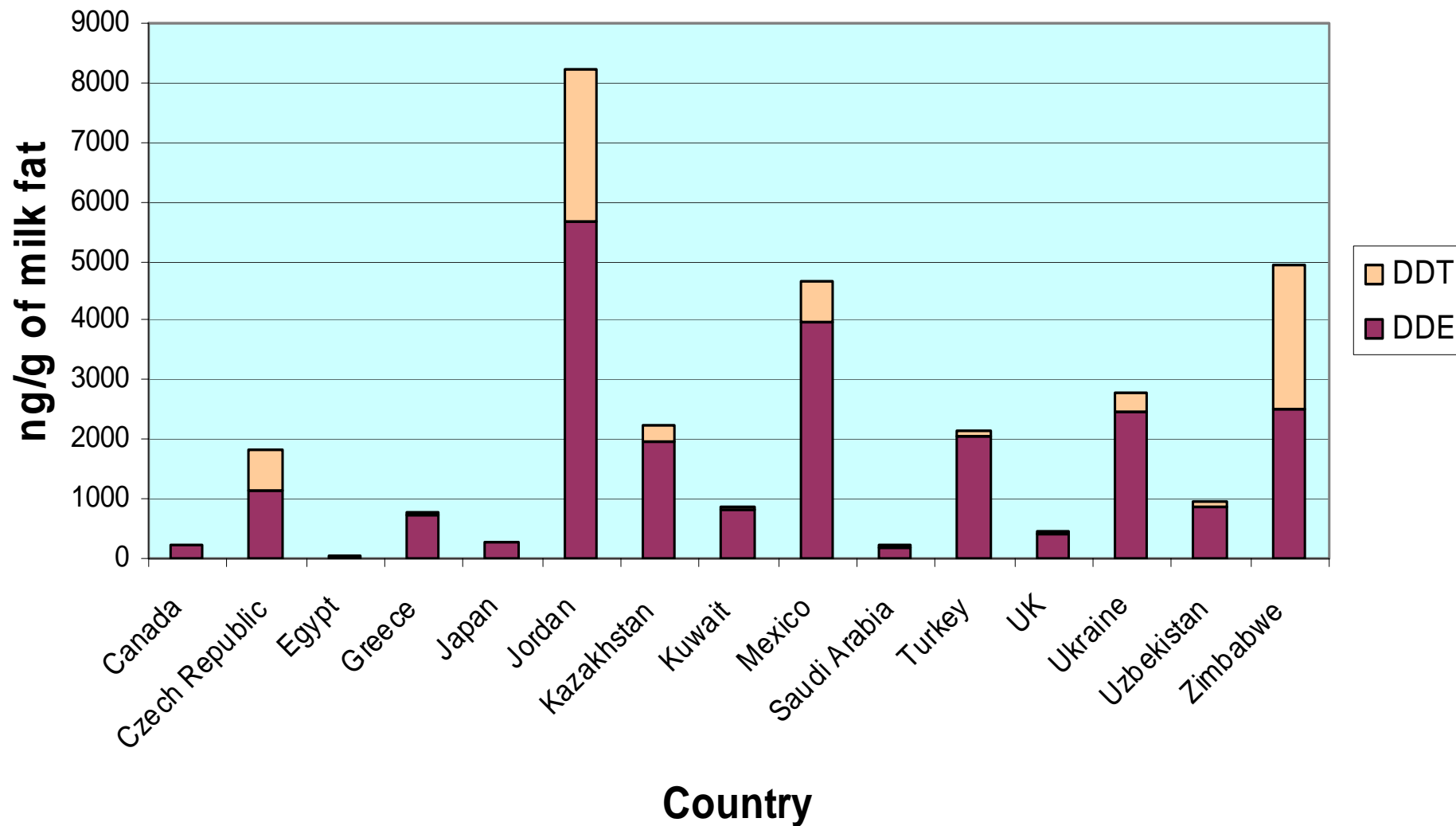
DDT/DDE



DDT/DDE

- Endocrine disruptor
- Pre-term labor
- Low birth rate
- Pregnancy loss
- Shortened period of lactation
- Possible Carcinogen
- Neurotoxicity from prenatal exposure
- Parkinson's Disease

DDT and DDE in Breast Milk Around the World (1990s)



DDT and non-malarial infant death

- Increase in preterm birth → 9% increase in total infant mortality.
- Decreased duration of lactation → 20% increase in total infant mortality because of infectious disease (diarrheal or respiratory)
- Estimated an increase in the number of infant deaths that is same magnitude as eliminating infantile malaria.

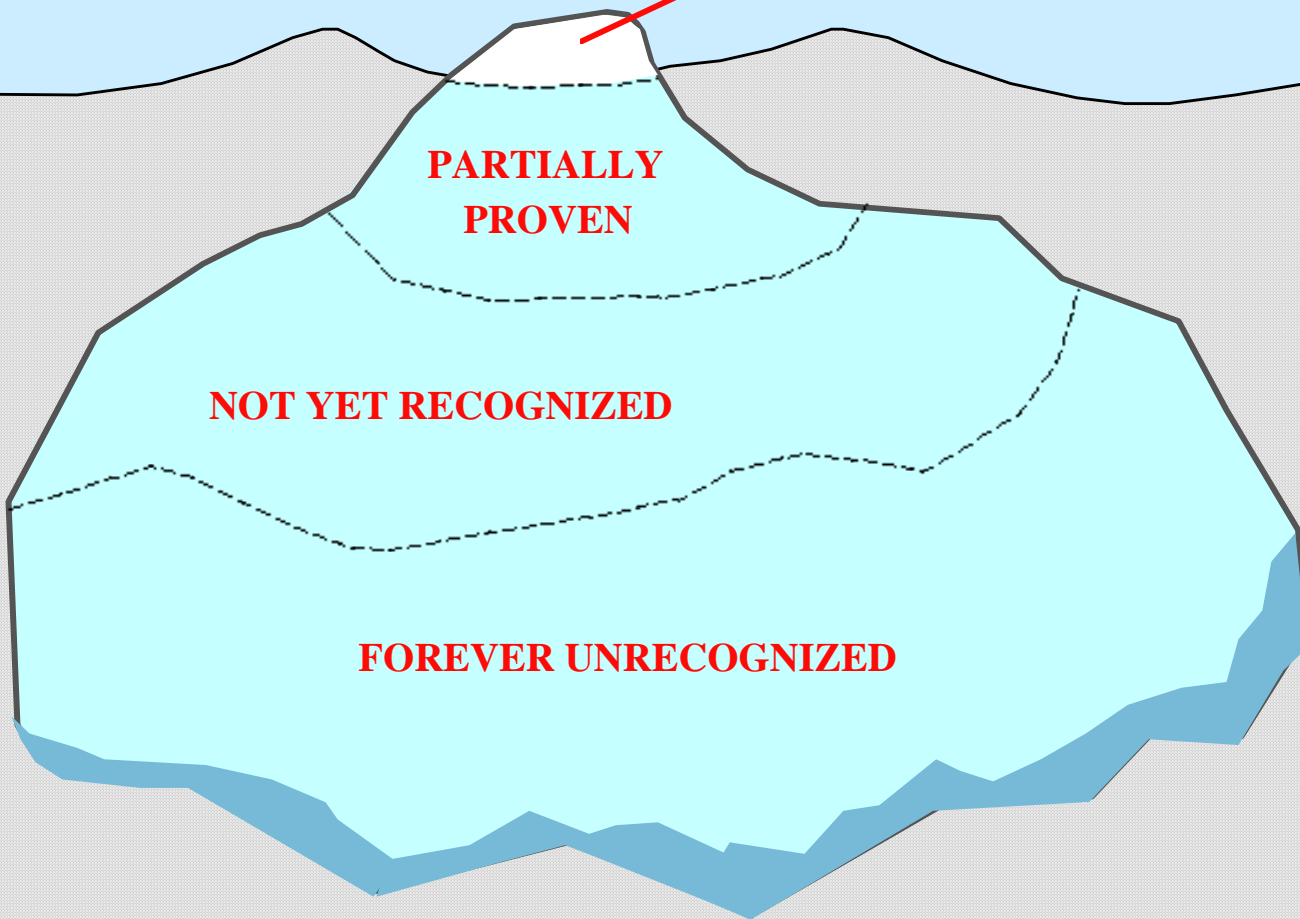
THE TOXIC ICEBERG

PROVEN HARM

PARTIALLY
PROVEN

NOT YET RECOGNIZED

FOREVER UNRECOGNIZED





A database linking chemical exposures to health conditions.

Authors: Sarah Janssen, MD, PhD, MPH
Ted Schettler, MD, MPH,
Gina Solomon, MD, MPH

Available on-line at
<http://database.healthandenvironment.org>



Goal of CHE database project

- Develop a database of health conditions linked to chemical exposures.
- Based on solid scientific evidence
- Addresses links from viewpoint of disease rather than an individual chemical.



Overview of CHE database

- Contains > 180 health conditions linked to occupational, environmental, or ambient exposures
- Sources were 3 major textbooks
and
>250 peer-reviewed scientific articles



Limitations of CHE database

- Addressed in introductory essay
 - Not comprehensive
 - Doesn't address dose, route, duration, or timing of exposures
 - Burden of disease
 - Categorization of chemicals



Strong evidence category

- Causal associations
- Large epidemiological studies
(prospective or retrospective cohort studies)
- Group 1 human carcinogens by the
International Agency for Research on Cancer
(IARC)



Good evidence category

- Smaller epidemiological studies (cross-sectional, case-series, or case-control)
- Chemicals with some human evidence and strong corroborating animal evidence
- IARC Group 2A chemicals,
 - limited evidence for causing cancer in humans and sufficient evidence in experimental animals.



Limited or conflicting evidence

- Weak associations by reports from only a few exposed individuals (case reports)
- Conflicting human epidemiological studies
- Studies demonstrating toxicity in animals.
- IARC Group 2B and EPA Group B2 chemicals
 - limited or inadequate evidence in humans and limited animal evidence of causing cancer



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CHE Toxicant and Disease Database

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University of California, San Francisco

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Natural Resources Defense Council; University of California San Francisco

Ted Schettler MD, MPH
Science and Environmental Health Network; Boston Medical Center

Human disease results from complex interactions among genes and the environment. Environmental exposures to chemical, physical, and biological agents may cause or contribute to disease in susceptible individuals. Personal lifestyle factors, such as diet, smoking, alcohol use, level of exercise, and UV exposure, often are a primary focus when considering preventable causes of disease. However, exposures to chemical contaminants on the job, at home, in the outdoors, and even *in utero*, are increasingly recognized as important and preventable contributors to human disease. These exposures are the focus of this project.

More than 80,000 chemicals have been developed, distributed, and discarded into the environment over the past 50 years. The majority of them have not been tested for potential toxic effects in humans or animals. Some of these chemicals are commonly found in air, water, food, homes, work places, and communities. Whereas the toxicity of one chemical may be incompletely understood, an understanding of the effect from exposures to mixtures of chemicals is even less complete. Chemicals may have opposing, additive, or even synergistic effects. One example of a synergistic effect is tobacco smoking coupled with asbestos exposure, which increases the risk of lung cancer by 25-fold—a risk much higher than that resulting from the sum of the risks of the individual agents.

Toxic effects of chemical agents are often not well understood or appreciated by health care providers and the general public. Some chemicals, such as asbestos, vinyl chloride and lead, are well established as causes of human disease. There also is good evidence to suggest increases in the incidence of some cancers, asthma, and developmental disorders can be attributed to chemical exposure, particularly in young children. Other diseases, such as ALS or Gulf War Syndrome have been hypothesized to be associated with chemical exposures, but the evidence is limited.

The effects of chemical exposures in humans are difficult to study because controlled human experimentation isn't ethically feasible. There is limited human data obtained from accidental exposures, overdoses, or studies of workers exposed occupationally. Environmental exposure studies in the general population also can be useful, though they often have limitations. Many diseases, such as cancer, may not appear until decades after an exposure has occurred making it difficult for causal associations to be identified. Exposure assessment, a critical step in environmental epidemiologic studies, is difficult. Retrospective exposure assessment usually requires estimates and considerable judgment and is subject to significant error. An individual's exposure may change over time, and exposures occur to multiple chemicals both in the home and work environments. It is difficult for individuals to remember what they have been exposed to and, moreover, most people are unaware of what their exposures were.

The effects of chemical exposures may vary, depending on the age of exposure (in utero, childhood, adult), the route of exposure (ingestion, inhalation, dermal), amount and duration of exposure, exposures to multiple chemicals simultaneously, and other personal susceptibility factors, including genetic variability.

Because of these challenges, most toxicity research is conducted in animal studies. Although animal studies are not the emphasis of this database, animal studies contribute important toxicological

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CHE Toxicant and Disease Database

The new CHE Toxicant and Disease Database is a searchable database that summarizes links between chemical contaminants and approximately 180 human diseases or conditions. Diseases and or toxicants can be viewed by clicking on the diseases below or by utilizing the search engine in the column on the right. For a full description of the database and its limitations, please click [here](#).

For questions or comments about the database, please contact Eleni Sotos at Eleni@HealthandEnvironment.org.

Displaying diseases in alphabetical order.

[<< PREVIOUS](#) [displaying records 1 - 25 out of 183] [NEXT >>](#)

- [Abnormal sperm \(morphology, motility, and sperm count\)](#)
- [Acroosteolysis \(vinyl chloride disease\)](#)
- [Acute hepatocellular injury \(Hepatitis\)](#)
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- [Altered sex ratio](#)
- [Altered time to sexual maturation \(accelerated or delayed puberty\)](#)
- [Alzheimer's](#)
- [Anemia \(including hemolytic\)](#)
- [Angiosarcoma \(hepatic\)](#)
- [Aplastic anemia](#)
- [Arrhythmias](#)
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CHE Toxicant and Disease Database

Breast cancer

Causes (strength of evidence):

- [Estrogens/DiES+ \(Strong\)](#)
- [ethyl alcohol \(ethanol\) \(Strong\)](#)
- [ionizing radiation \(Strong\)](#)
- [Tobacco Smoke \(Active smoking\) \(Strong\)](#)
- [Tobacco smoke \(Secondhand\)% \(Strong\)](#)
- [Aromatic amines \(Good\)](#)
- [B-naphthylamine \(Good\)](#)
- [benzidine \(Good\)](#)
- [ethylene oxide \(Good\)](#)
- [PAHs \(Good\)](#)
- [PCBs* \(Good\)](#)
- [Progestins^ \(Good\)](#)
- [Solvents \(Good\)](#)
- [tetrachloroethylene \(PCE\) \(Good\)](#)
- [1,1-dichloroethane \(Limited\)](#)
- [1,2,3-trichloropropane \(Limited\)](#)
- [1,2-dibromoethane \(Limited\)](#)
- [1,2-dichloroethane^ \(Limited\)](#)
- [1,2-dichloropropane \(Limited\)](#)
- [1,3-butadiene \(Limited\)](#)
- [acrylamide# \(Limited\)](#)
- [acrylonitrile \(Limited\)](#)
- [Agent Orange \(Limited\)](#)
- [aldrin \(Limited\)](#)
- [atrazine \(Limited\)](#)
- [benzene \(Limited\)](#)

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■ Dioxins/TCDD [Limited]
■ Electromagnetic fields [Limited]
■ Herbicides [Limited]
■ Hydrazines ^ [Limited]
■ methylene chloride ^ [Limited]
■ mirex ^ [Limited]
■ Organochlorine pesticides [Limited]
■ oryzalin [Limited]
■ Pesticides [Limited]
■ Phenoxyacetic herbicides [Limited]
■ PhIP (2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine) [Limited]
■ propazine [Limited]
■ simazine [Limited]
■ Solvents [Limited]
■ styrene [Limited]
■ tribenuron methyl [Limited]
■ trichloroethylene (TCE) [Limited]
■ vinyl chloride [Limited]

Notes

+ - Group 1 human carcinogen, # - Group 2A human carcinogen, ^ - Group 2B human carcinogen (IARC)
Occupational exposure to vehicular exhaust was associated with an increased risk of breast cancer in males. Cigarette smoke, especially second-hand smoke, contains high levels of PAHs. Eleven constituents of cigarette smoke have been found to cause mammary gland carcinogens in animals. These chemicals include benzo[a]pyrene, dibenzo[a,l]pyrene, 2-toluidine, 4-aminobiphenyl, 2-amino-3-methylimidazoquinoline, 2-amino-1-methyl-6-phenylimidazopyridine, butadiene, isoprene, nitromethane, ethylene oxide, and benzene. % - secondhand smoke exposure in pre-menopausal women has been associated with breast cancer, but not in post-menopausal women. *-Genetic polymorphisms in the estrogen metabolizing enzyme, CYP1A1, may predispose some women to breast ca after PCB exposure. Women with a genetic variant in the NAT enzyme system (slow acetylators) have a 70% increased risk of breast cancer if they smoke. In contrast, the opposite genetic variant, or fast acetylators, have a doubling of breast cancer risk from exposure to second hand smoke.

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