

Environmental Pollutants and Chronic Disease in Children: The New Pediatric Morbidity

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Overview

- There is a new set of chronic illnesses in children that are likely attributable in part to environmental pollutants
- The incidence of these illnesses is on the rise (even though mortality may be dropping in some cases).
- The etiology of these illnesses is complex
- They are largely preventable

The changing nature of illness in U.S. Children

- Infectious disease largely conquered in developed countries
 - Safe drinking water, food, sanitary hygiene
 - Vaccines, antibiotics, improved nutrition
 - Incidence of most infectious diseases down or eliminated – measles, cholera, smallpox
- Life expectancy today is nearly two decades more than at turn of the century

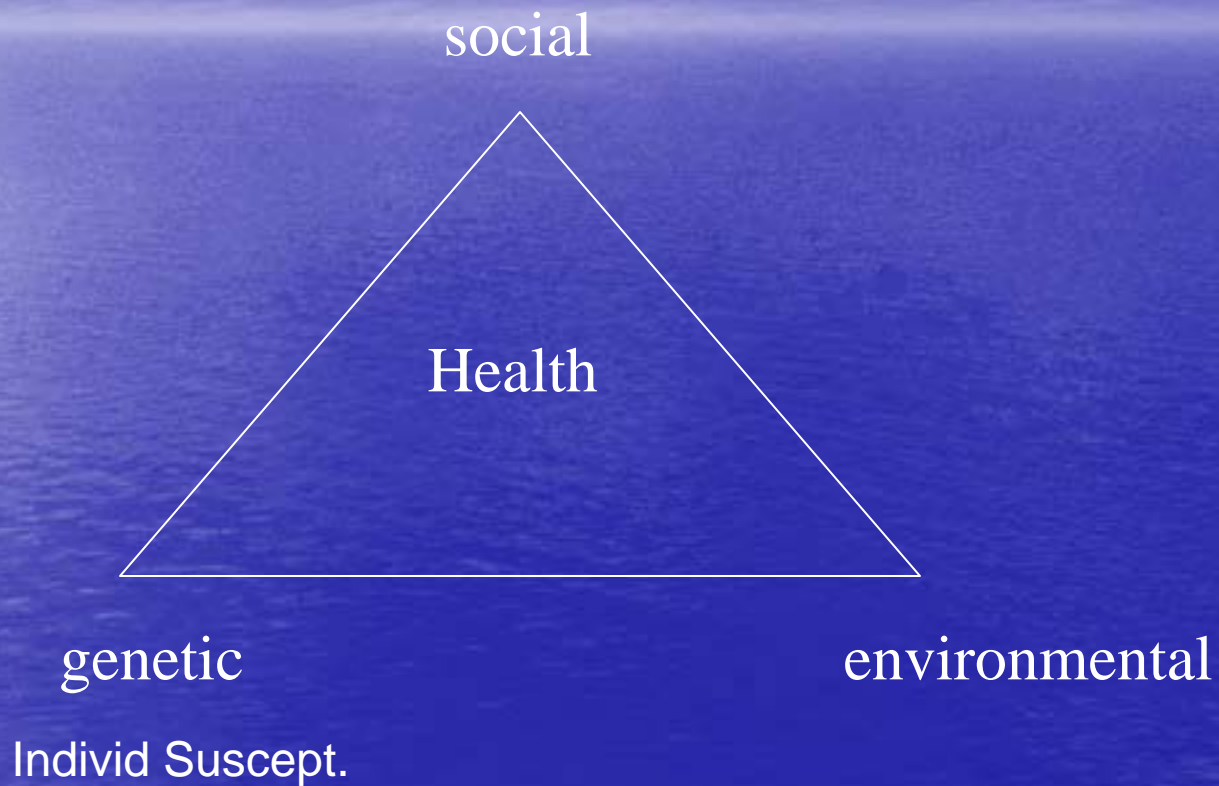
But...

- New hazards created with control of “older” ones
 - Chemical exposures
 - Contaminated sites
 - Pollutants from cars, power plants, every day products
- New understandings about how exposures during vulnerable windows of development can affect health
- Increasing evidence of links to environmental factors: The ABCs – Asthma and Allergies; Learning and Behavioral Disorders; and Cancer (but also adverse reproductive outcomes).
- Clearly lifestyle and genetic factors still play an important role

“Old” and “Emerging” Pollutants

- Old
 - Lead, mercury, PCBs, DDT (and other organochlorines), PAH's, NOx, SOx, dioxins, organophosphate pesticides, solvents
- New
 - PBDEs, phthalates, PFOA, bisphenol-a, endocrine disruptors
- Though still lingering problems – ie lead in kids lunch boxes and jewelery

Multiple Interacting Factors



Cancer and Environment: the Swedish Study

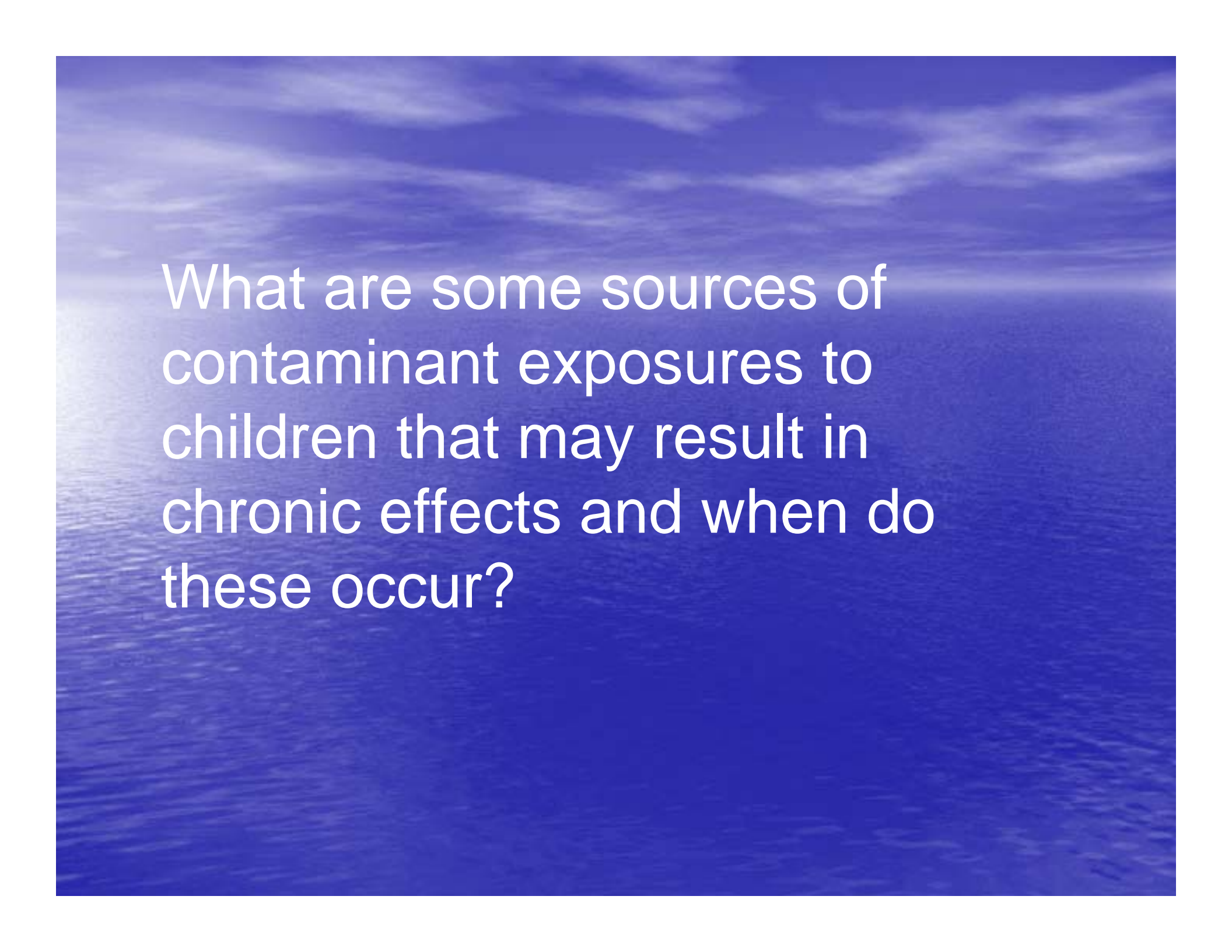
- A study of 45,000 twins, 10,800 cancers
- Statistically significant heritable components for only three cancers: breast, prostate, colorectal
- Breast - 27% of the risk may be due to inherited factors (range 4-41%)
- Prostate – 42% may be due to inherited factors (range 29-50%)
- **Most cancers are mostly related to environmental factors.**

(New England Journal of Medicine, July 2000)

Cancer and the Environment: the Swedish Study

- The importance of early life events:
 - Breast, prostate, testicular cancer
 - The Swedish study:
 - 9.6 million people
 - Environmental factors more important than genetic
 - Cancer risk largely established during first 20 yrs. of life

(Intl J Cancer, 2002)



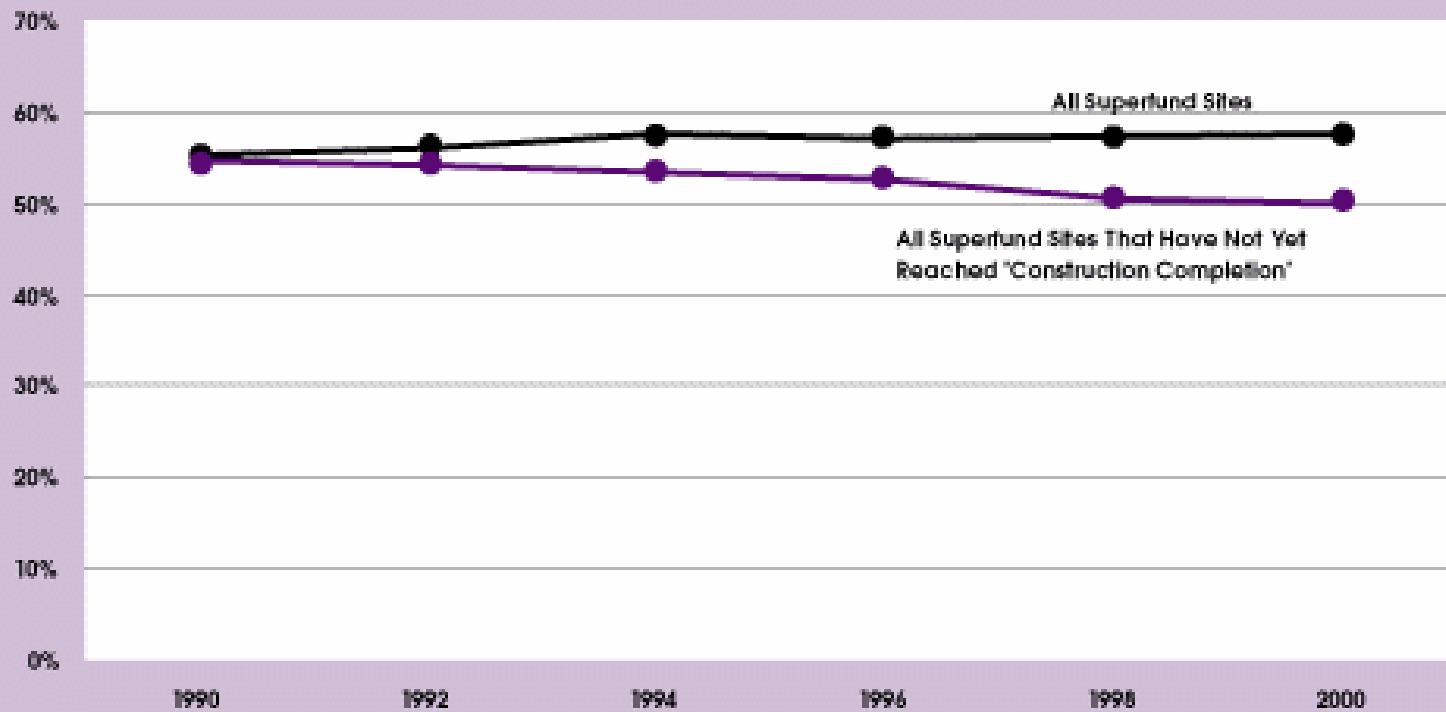
What are some sources of contaminant exposures to children that may result in chronic effects and when do these occur?

Sources of exposure that can result in pediatric environmentally related illness

- Pre-conception (male/female)
 - Workplace
 - Home chemical use
 - Air toxics
- Pre-natal
 - Workplace
 - Household exposures/environmental exposures
- Post-natal (home and school environments)
 - Food (including breastmilk) from pesticides/chemicals/pharmaceuticals
 - Soil/Dust
 - Everyday products – sucking/poisoning
 - Water
 - Air
 - Occupational and from parents
- Initial body burden (cord blood)
- What are the root sources of these contaminants?

Measure E9

Percentage of children living in counties with Superfund sites

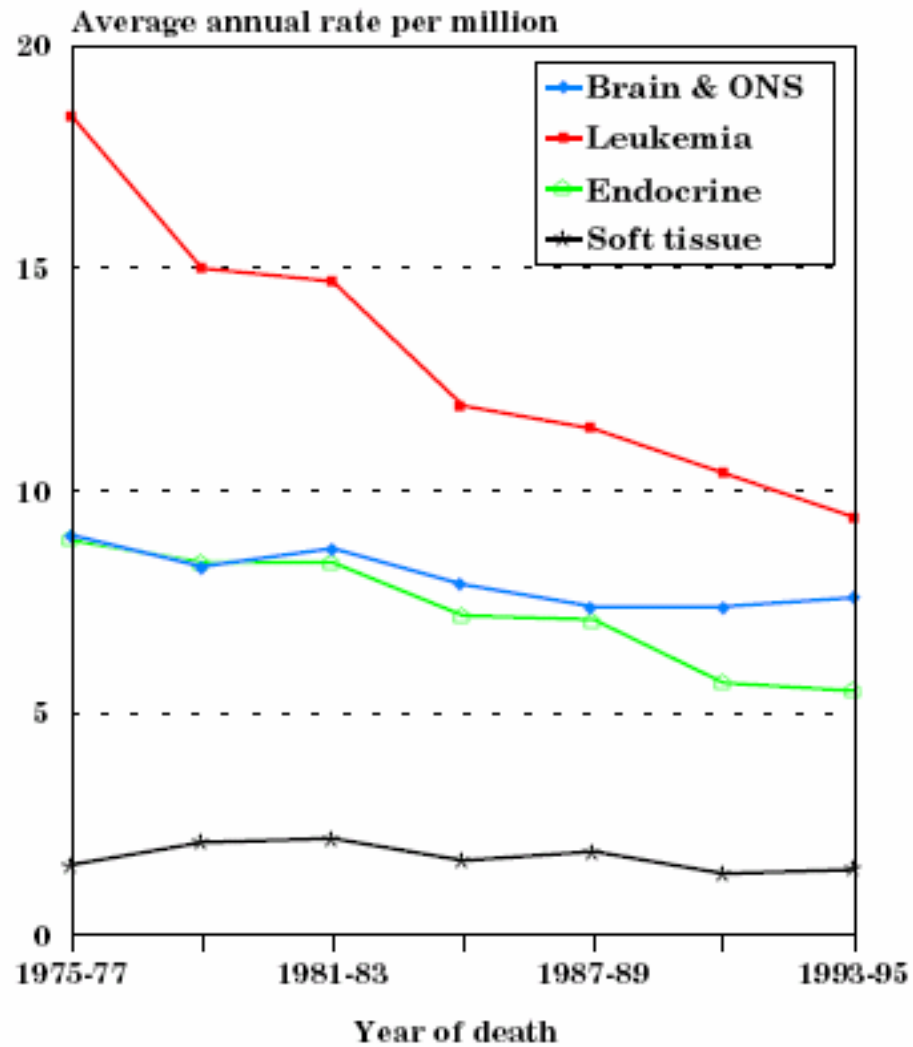


SOURCE: Environmental Protection Agency, Superfund NPL Assessment Program (SNAP) Database

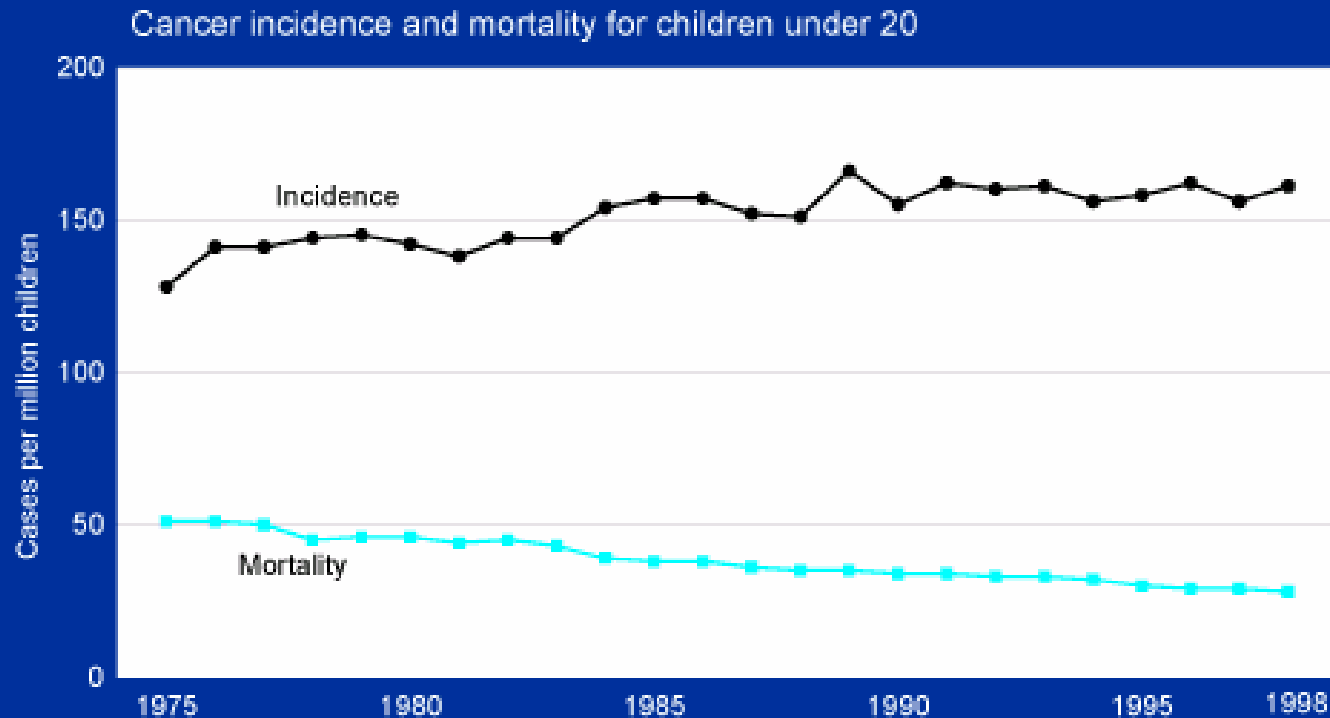
Childhood cancer

- Most fatal disease in US children – about 1500 deaths per year
- 8000 children under 15 are diagnosed with cancer each year.
- 21% increase in incidence over 20 year period.
- Leukemia and CNS cancers account for about 50% and diagnosis generally under age of 5. Also some of the highest increases in incidence.
- As much as 90% of childhood cancer may be attributable to environmental exposures – ie as many as 7200 new cases per year.
- If improved diagnosis accounted for increasing incidence then would see rates flattening.

**Figure XIV.6: Trends in age-specific cancer mortality rates by type, age <5, all races, both sexes
United States, 1975-95**



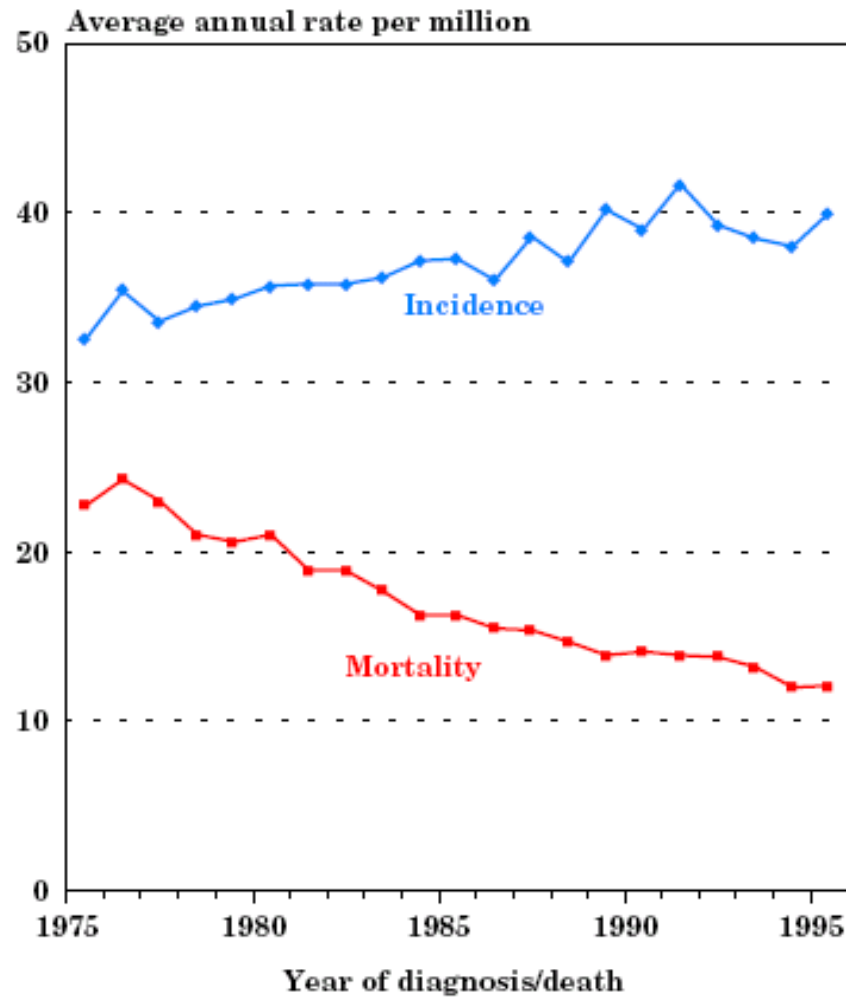
Source: NCI



SOURCE: U.S. Environmental Protection Agency, 2003. America's Children and the Environment: Measures of Contaminants, Body Burdens, and Illnesses. www.epa.gov/envirohealth/children

DATA: Incidence data from National Cancer Institute, Surveillance, Epidemiology and End Results Program; mortality data from Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System

Figure XIV.3: Trends in childhood leukemia age-adjusted* rates, age <20, all races, both sexes SEER incidence, and US mortality, 1975-95



*Adjusted to the 1970 US standard population

Source: NCI

Potential Environmental Carcinogens

- Foods (aflatoxin, other fungal toxins);
- Food additives (some food dyes)
- Habits (tobacco, alcohol)
- Drugs (Tamoxifen, estrogen, phenobarbital, oxazepam, DES, chemotherapeutic agents)
- Minerals (asbestos, silica, arsenic, chromium, cadmium)
- Pesticides (dichlorvos, ethylene oxide, pentachlorophenol)
- Solvents (benzene, trichloroethylene, formaldehyde)
- Byproducts (dioxins, furans, PAHs, diesel exhaust)
- Other chemicals (aniline dyes, acrylonitrile, butadiene)
- Ionizing radiation

Studies on childhood cancer and chemicals

- Pesticides
 - Prenatal – mothers using pesticides during pregnancy; farmworker exposure
 - Child exposure to home use pesticides
- Solvents
 - Preconception – benzene, chlorinated solvents
 - Prenatal – workplace, contaminated drinking water
 - Post-natal – drinking water
- Hydrocarbons and byproducts
 - Paternal workplace exposure
 - Child exposure to dioxins
 - Hazardous air pollutants (PAHs?)
- Supported by laboratory and cellular studies.

Household exposure to pesticides and risk of childhood acute leukaemia

AUTHOR Menegaux, F et al, Occupational and Environmental Medicine, v63 n2, February 2006, pp131-134

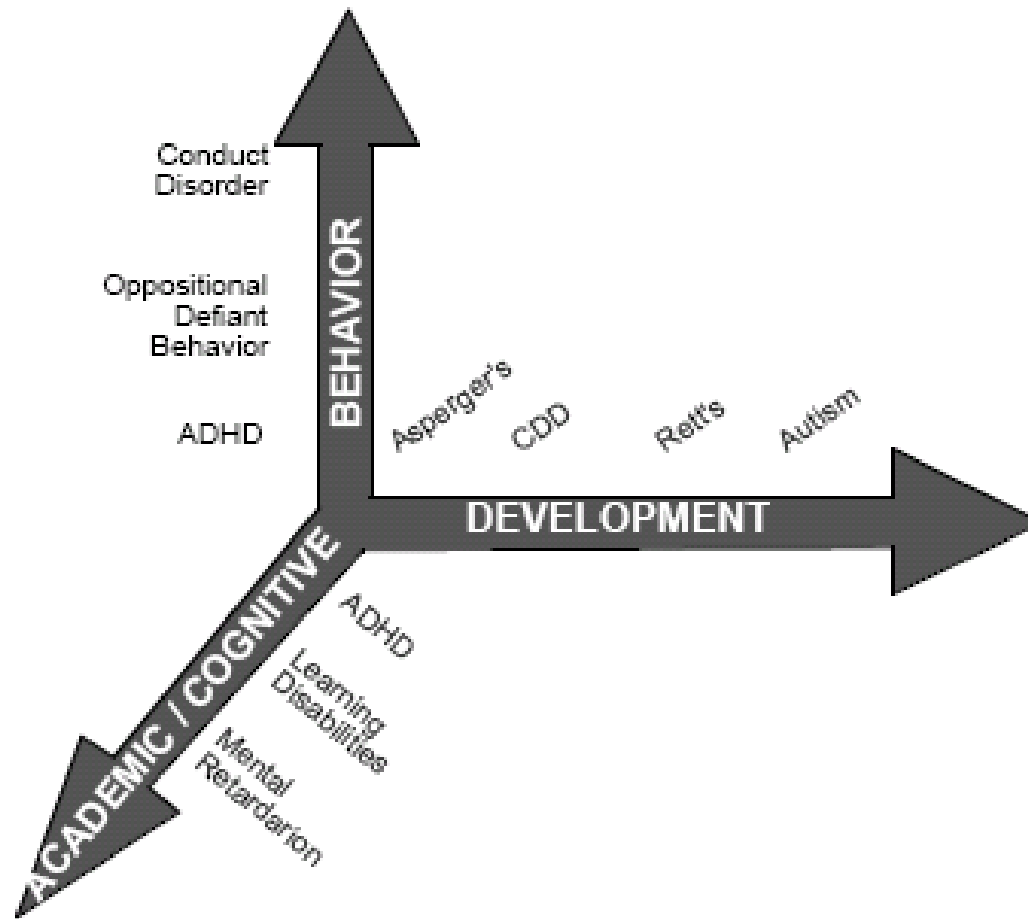
Objectives: To investigate the relation between childhood acute leukaemia and household exposure to pesticides.

Results: Acute leukaemia was observed to be significantly associated with maternal home insecticide use during pregnancy (OR = 1.8, 95% CI 1.2 to 2.8) and during childhood (OR = 1.7, 95% CI 1.1 to 2.4), with garden insecticide use (OR = 2.4, 95% CI 1.3 to 4.3), and fungicide use (OR = 2.5, 95% CI 1.0 to 6.2) during childhood. Insecticidal shampoo treatment of pediculosis was also associated with childhood acute leukaemia (OR = 1.9, 95% CI 1.2 to 3.3).

Neurodevelopmental problems

- Nearly 12 million children under age 18 in the US suffer from one or more developmental disabilities - 17% of US children
- Learning disabilities alone affect 5-10% of children in public schools
- ADHD conservatively affects 3-6% of all school children; may be higher
- Marked increase in autism reported in CA and MA
- See Physicians for social responsibility: In Harms Way, 2001.

Spectrum of Developmental Disorders



Source: PSR
In Harms Way

Lead, alcohol, nicotine

- Recognized as neurodevelopmental toxicants for years
- Alcohol – hyperactivity, cognitive deficits
- Nicotine – IQ deficit, learning and attention deficits
- Lead – impaired IQ, learning, attention; hyperactivity, impulsiveness, aggression; failure to complete school, trouble with the law (effects as low as 2.5 ug/dl). No known threshold for safety

Known and Suspect Neurodevelopmental Toxicants

- Extensive data on effects of lead, mercury, polychlorinated biphenyls (PCBs), alcohol, nicotine, ethanol.
- Less extensive but substantial data on neurotoxic pesticides, solvents other than alcohol.
- Still fewer data on other compounds including manganese, fluoride.

Toxicants and their Health Effects

Toxicant	Health Effects/ Characteristics
Metals	
Cadmium – H, A	Learning disabilities Decreased IQ Motor dysfunction Hyperactivity Hypoactivity
Lead – H, A	Learning disabilities IQ deficit Attention deficit Impulsivity Violence Hyperactivity Aggression
Manganese – H, A	Brain damage Motor dysfunction Compulsive behavior Memory impairment Hyperactivity Learning disabilities Attention deficit
Mercury – H, A	Visual impairment Learning disabilities Attention deficit Motor dysfunction Memory impairment (minimal) <i>At higher levels:</i> Smaller brain size, cellular distortions in brain Mental retardation
Solvents	
Ethanol (Alcohol) – H, A	Learning disabilities Attention deficits Memory impairment Behavioral disorders Eating and sleeping disorders Lower brain weight Craniofacial, limb and cardiovascular abnormalities associated with various growth and developmental delays Mental retardation
Styrene - A	Decreased activity Decreased avoidance behavior <i>In conjunction with dietary protein deficiency:</i> Lower brain weight, Hyperactivity

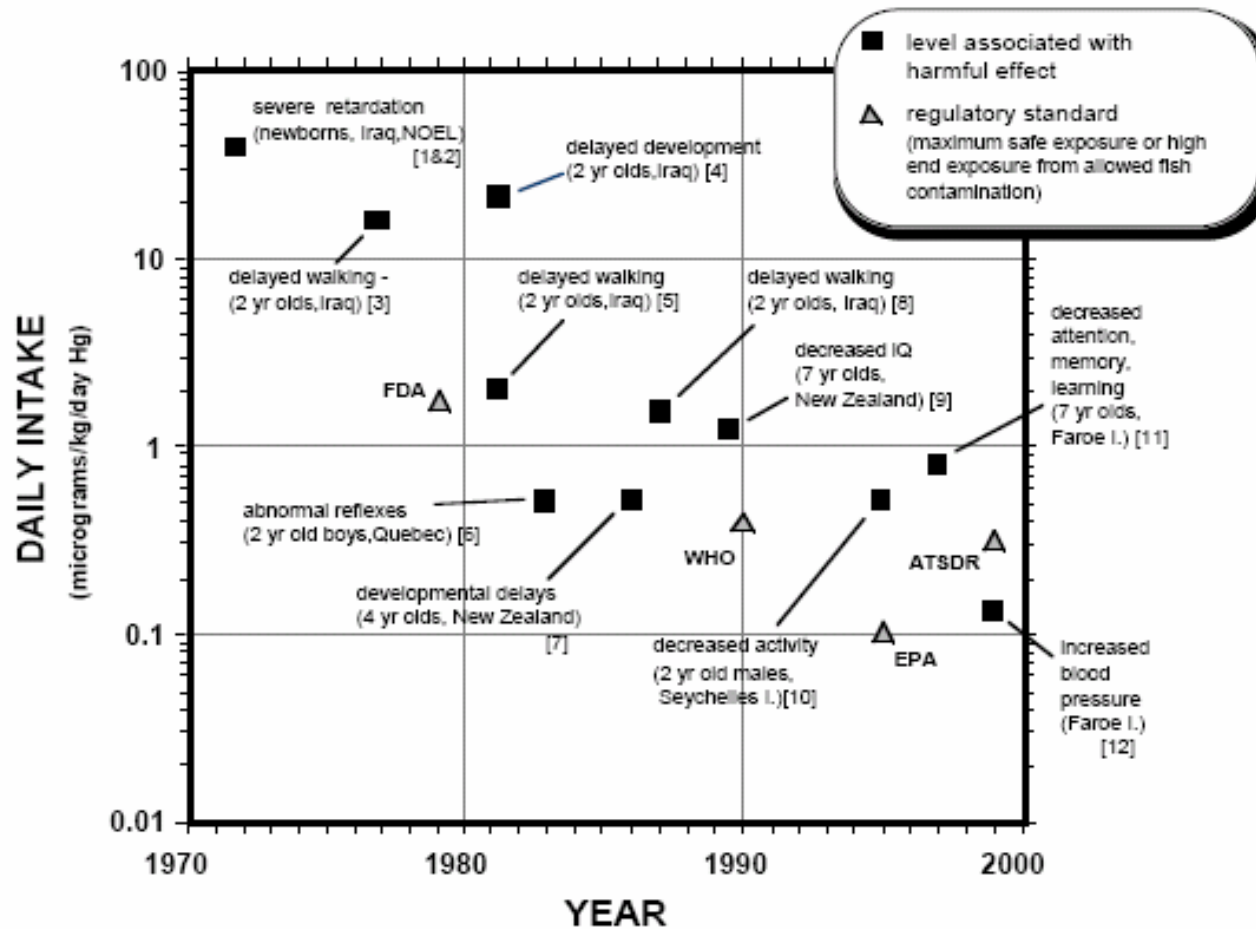
Toxicant	Health Effects/ Characteristics
Solvents	
Toluene – H, A	Learning disabilities Speech deficits Motor dysfunction Craniofacial abnormalities
Trichloroethylene - A	Increased exploratory behavior Hyperactivity
Xylene - A	Motor dysfunction Learning disabilities Memory impairment Decreased brain weight
Pesticides	
Organochlorines DDT - A Mixture – H	Hyperactivity Decreased stamina Decreased coordination Decreased memory Decreased ability to draw familiar objects
Organophosphates (including DFP, chlorpyrifos (Dursban), diazinon) - A	Developmental delays Hyperactivity Behavioral disorders Motor dysfunction
Pyrethroids (including bioallethrin, deltamethrin, cypermethrin) - A	Hyperactivity
Other	
Nicotine – H, A	Hyperactivity Learning disabilities Developmental delays in cognitive functions
Dioxins – H, A	Learning disabilities
PCBs – H, A	Learning disabilities Attention deficit Memory impairment Hyperactivity Psychomotor dysfunction
Fluoride – A H	Hyperactivity Decreased IQ (ecologic studies)

H= Human studies,
A= Animal studies

Notes:

1. Learning disabilities include dysfunctions in listening, speaking, reading, writing, spelling or calculations.
2. Only neurodevelopmental, learning or behavioral effects of toxicants, or physical impairments that lead to them, are listed.
3. Chart information is synthesized from Chapter 6. Please see this chapter for references to studies on these chemicals.

Declining Threshold of Harm for Mercury



As we learn more – we learn that exposures may affect health at even lower levels

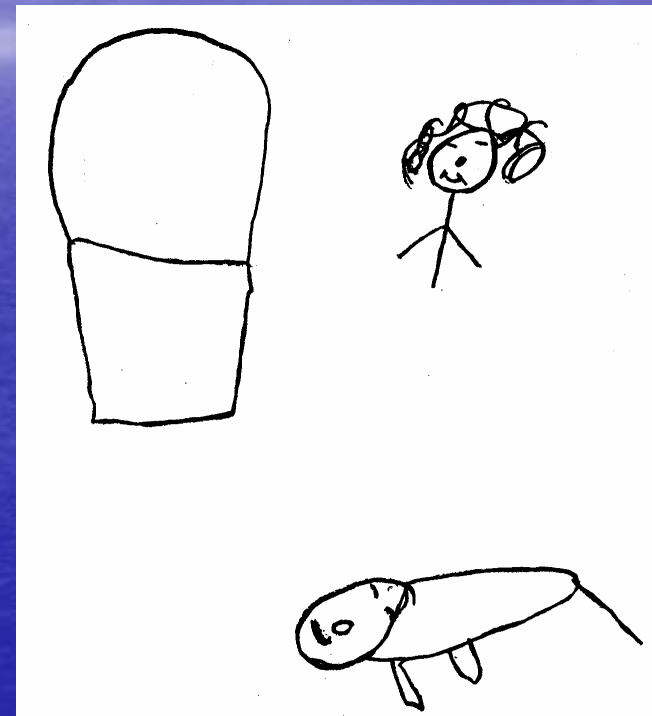
Source: PSR In Harms Way

Subtle, Hard to Detect Neurological Effects

Foothills



Valley

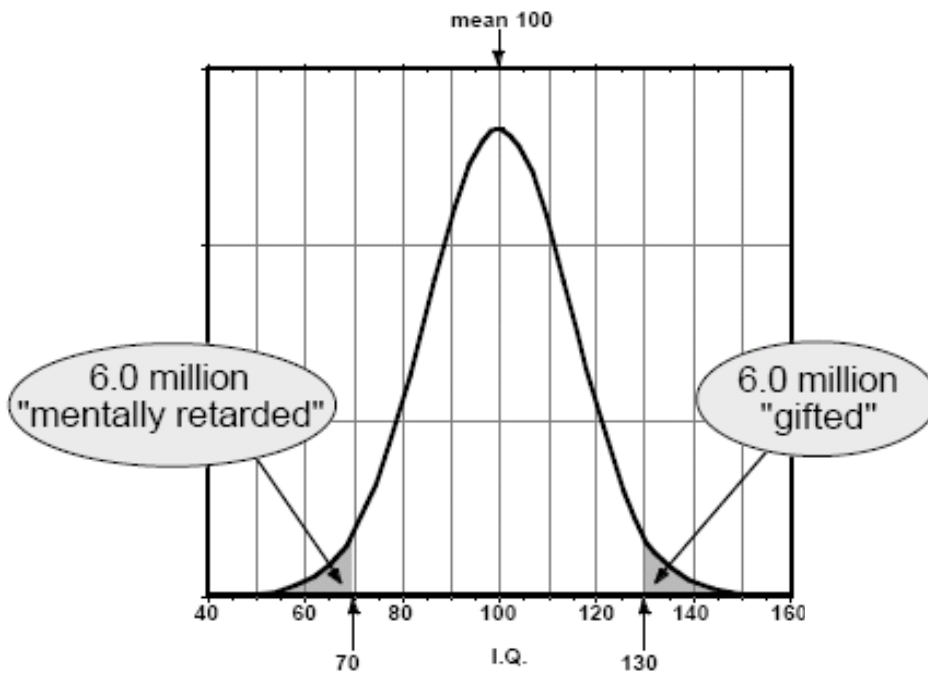


Yaqui Indians – Difference between children exposed to pesticides and not exposed – from Guillette, 2002

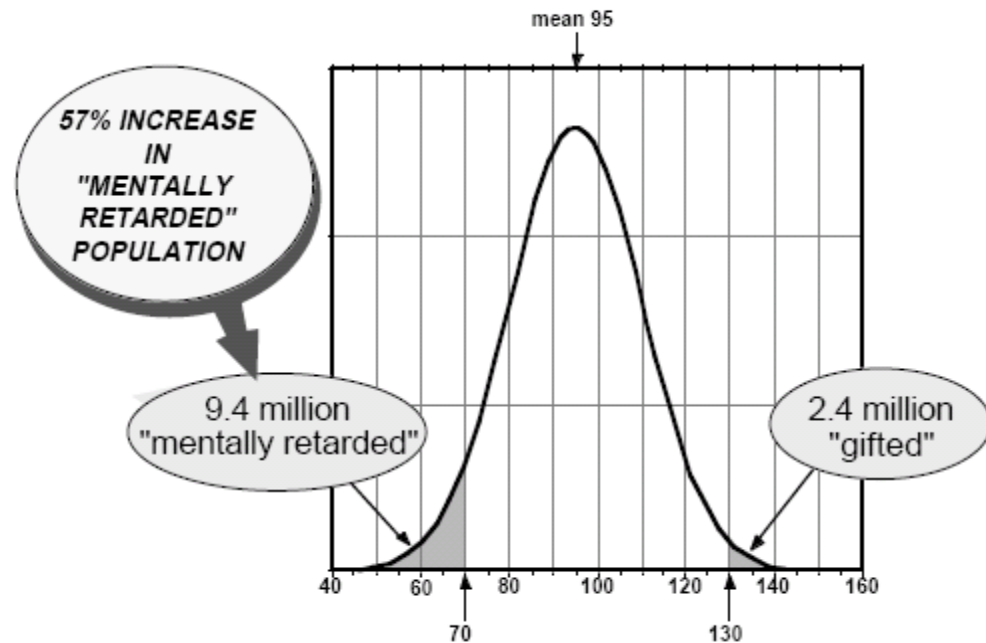
Example: Mercury

- Multiple exposures – power plants, emissions, discarded materials
- Neurological effects known for centuries (mad hatters disease)
- Effects on children known since 1940s – Minimata, Iraq, Faroe Islands
- 1.16 million women of childbearing age eat enough mercury contaminated fish to pose a risk of harm to their children
- About 10% of US women of childbearing age have levels of mercury in their urine within $1/10^{\text{th}}$ of the level estimated to affect cognitive function in offspring.
- Women of childbearing age being warned to avoid fish

Original IQ Distribution



Effect of a 5 Point Shift in Average IQ



So why does a little IQ drop in an individual matter??

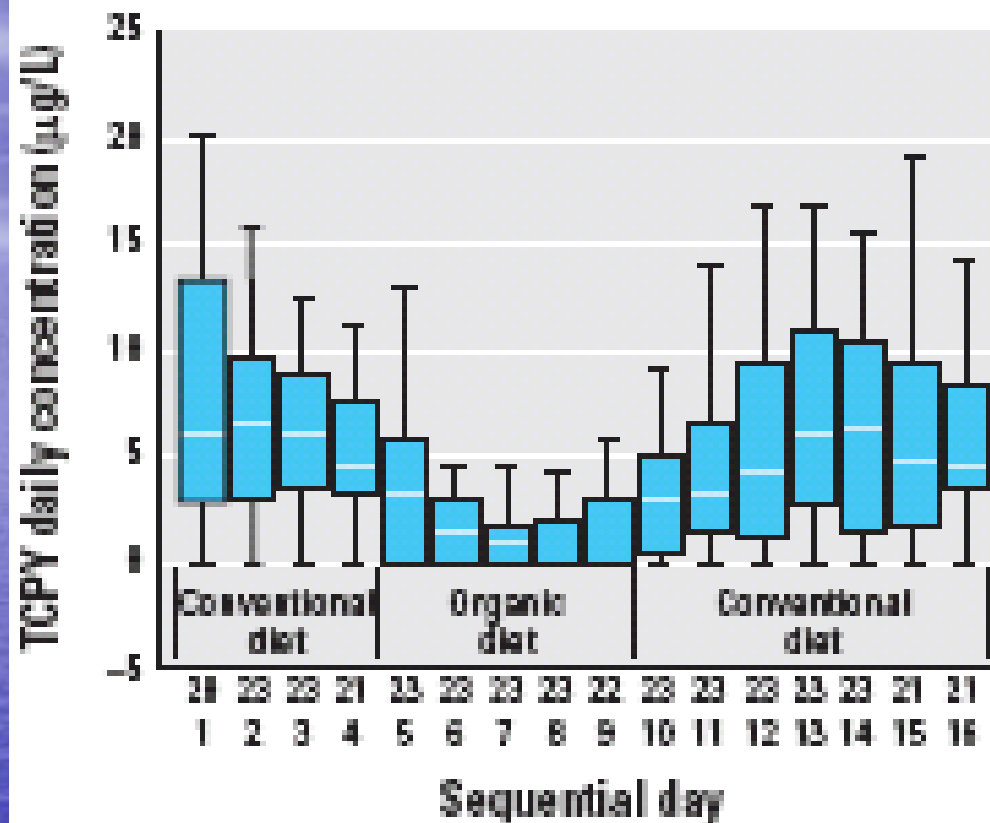
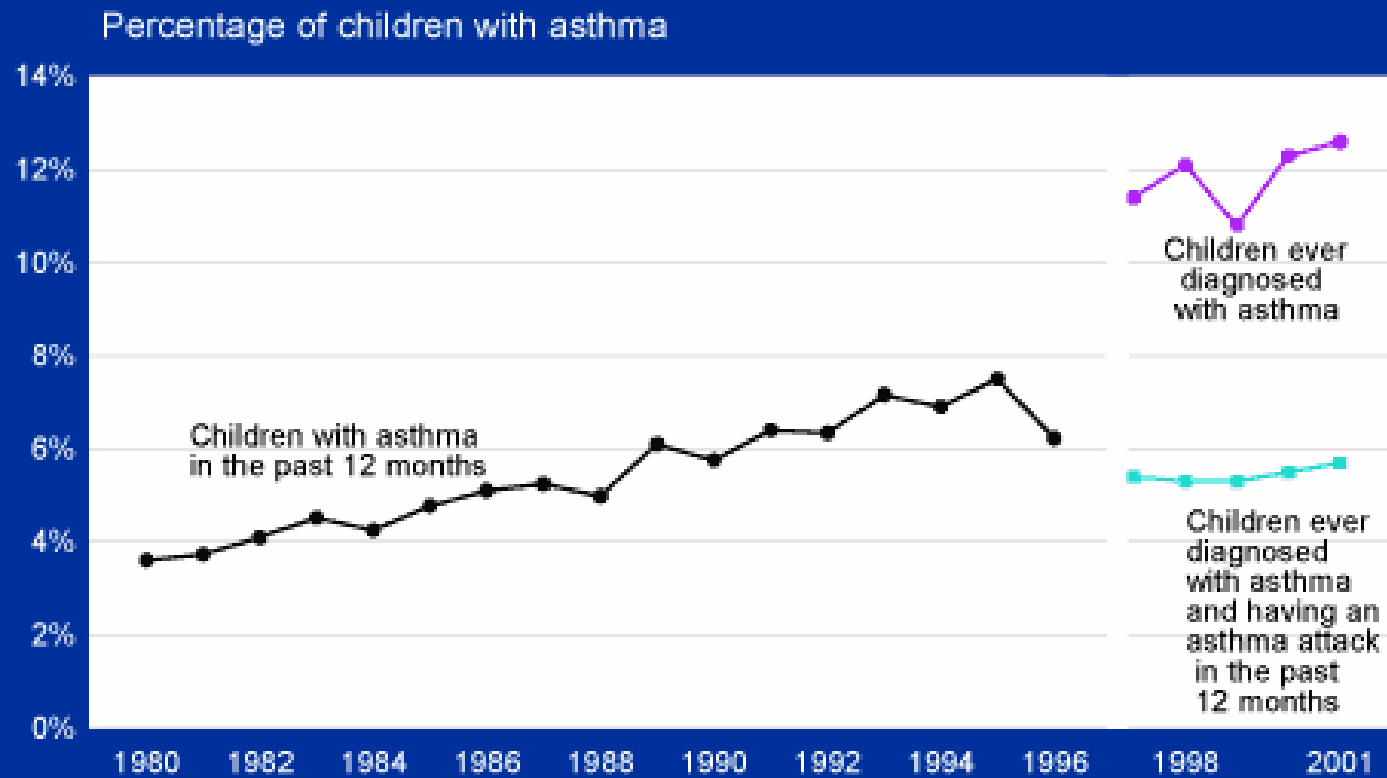


Figure 2. Box plots of DWWA of TCPY concentrations in 23 children 3–11 years of age for 15 consecutive days in which conventional and organic diets were consumed. The top row of numbers on the *x*-axis represents numbers of children.

Asthma

- A multifactorial disease that has a genetic basis and is exacerbated by a wide range of factors including infections, allergens, tobacco smoke, and environmental toxicants.
- Mortality among children from asthma has doubled over the past decade
- Self-reported prevalence rates for asthma among children ages 0-4 years increased by 160% from 1980 to 1994; rates among children ages 5-14 years increased by 74%. Highest prevalence (up to 35%) in inner city, minority children.
- Over 160,000 children aged 0-14 years are hospitalized for asthma annually. Among all age groups, children aged 0-4 years had the highest hospitalization rate in 1993-1994 (49.7 hospitalizations per 10,000 persons)
- Connections to Allergies?

Measure D1



SOURCE: U.S. Environmental Protection Agency, 2003. America's Children and the Environment: Measures of Contaminants, Body Burdens, and Illnesses. www.epa.gov/envirohealth/children

DATA: Centers for Disease Control and Prevention, National Center for Health Statistics, National Health Interview Survey

Note: The survey questions for asthma changed in 1997; data before 1997 cannot be directly compared to data in 1997 and later.

Asthma Etiology – Interaction of Multiple Factors

1. **Predisposing factors**, such as atopy—a tendency to have an allergic reaction to foreign substances.
2. **Environmental causal factors**, such as indoor air pollutants (e.g., environmental tobacco smoke and house dust mite antigen) and outdoor air pollutants (e.g., ground-level ozone).
3. **Aggravating factors**, which increase the frequency and/or severity of asthma episodes and include environmental tobacco smoke, certain indoor air allergens, outdoor air pollutants, including PM and ground-level ozone, and respiratory infections.

While heredity plays a role in the development of asthma, it alone cannot adequately explain the large increase in asthma prevalence

Asthma – Environmental Factors (allergens, irritants)

Indoor allergens -----	dust mites, cockroach feces, pet antigens, mold, latex
Outdoor allergens -----	pollen
Air pollution ----- (indoor and outdoor)	diesel exhaust particles (and other particulate matter), nitrogen oxides, SO ₂ , ozone, fragrances, building and cleaning materials, ETS
Pesticides ----- -	organophosphates, carbamates, pyrethrins
Isocyanates	
Occupational irritants and allergens	

See <http://www.cleanairstandards.org/article/articleview/454/1/15/>

Adverse reproductive outcomes

- Reproductive toxicity – broad term including:
 - Infertility - abnormal functioning of the male or female reproductive system
 - Spontaneous abortion
 - Low birth weight/pre-term birth
 - Birth defects
 - Developmental toxicity – developmental delays, etc.

Environmental exposures that may affect fertility/reproduction

- Heat
- Ionizing radiation
- Physical stress (heavy lifting, exercise?)
- Viruses (rubella, cytomegalovirus)
- Smoking, alcohol use, caffeine(?)
- Illicit drugs
- Toxic substances (chemicals/heavy metals)
- STDs

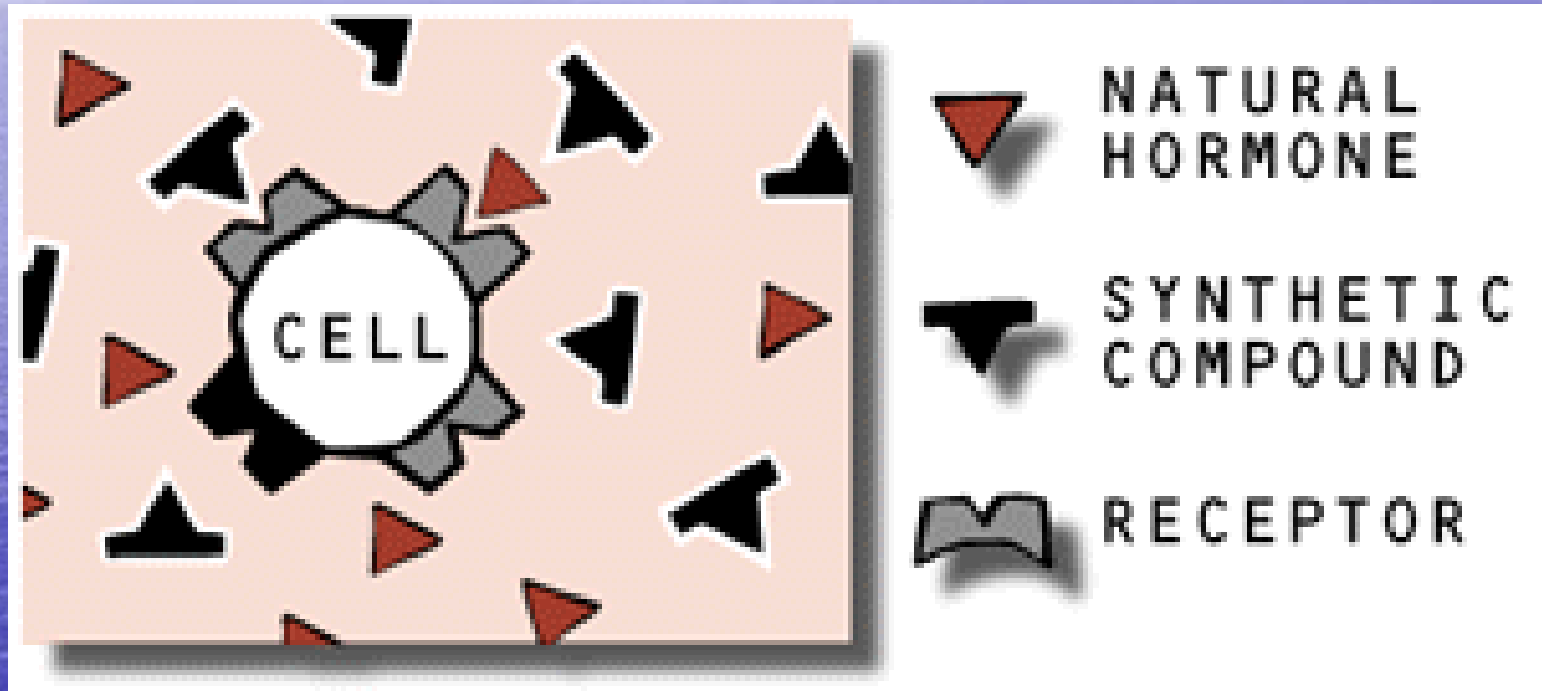
Chemical agents associated with adverse reproductive outcomes in laboratory experiments and/or humans or wildlife

- Pesticides (DDT, DBCP, diaznonon, dicofol)
- Anesthetic gases
- Industrial chemicals
 - Solvents (Perc, TCE, toluene, glycol ethers, kepone)
 - Heavy metals (lead, cadmium, mercury, arsenic)
 - Byproducts (dioxins/PAHs)
 - Plastics (monomers/additives, styrene, phthalates)
 - PCBs
 - Sterilization chemicals (ethylene oxide)
- Pharmaceuticals/antineoplastic agents/food additives(?)

Ways in which environmental exposures can affect fertility

- Pre-implantation/post-implantation
 - Impacts on fertility and reproductive capacity of adults
 - Impacts on next generations – structural/hormonal/behavioral
- Direct damage to the structure of cells
- Interference with biochemical processes necessary for normal cell function
- Through similarity to normally present compounds – hormone mimics – trigger a cascade of inappropriate events or block events required for normal function.
- Indirect action – through biotransformation to more toxic metabolites

Hormone Disruption – An emerging area of concern for impacts of chemicals



Mechanisms through which environmental exposures can affect fertility/reproduction

- Testicular/spermatotoxicity
- Interference with ovulation
- Interference with implantation of fertilized egg
- Interference with corpus luteum function
- Direct fetal toxicity (impacts on next generation)

Example: 1,2-dibromochloropropane (DBCP)

- 1961 – laboratory studies show testicular toxicity at low doses.
- 1967 – Single worker's compensation claim. 1977 – Small group of workers at plant notice that few had recently fathered children (large impacts in Latin America).
- Significant dose-related difference in median sperm counts and frequency of azoospermia observed between exposed/non-exposed workers.
- Seminiferous tubules are site of action and spermatogonia the target cell. No other abnormal physical or laboratory findings.
- Spermatogenic function recovered in those less severely affected though many azoospermic men remained azoospermic.

Example – Alligators in Lake Apopka, FL

- Dramatic decline in alligator populations in '80s following pesticide spill (dicofol)
- Mortality in surviving newborns
- Demasculinization of males and superfeminization of females
- Abnormal genitals in males (penises 1/3 normal size and some with no penis or ovaries).
- Similar hormone abnormalities and reproductive dysfunction found in other FL lakes. Also problems among panthers, other mammals, birds, and fish in other regions.

Example – Trends in male reproductive system abnormalities

- Some studies suggest that sperm counts have declines up to 40% over the past 50 years. Large meta-analyses. One French study found a 2.1% decline in sperm count per year during last 2 decades
- Doubling of incidence of undescended testicles (some epidemiologic links to environmental exposure)
- Doubling of hypospadias rates in the US in the 1970s and 1980s in the US (cause is unknown)
- Decreasing male to female sex ratio in some industrialized countries? (evidence from Seveso accident and DBCP spraying and wildlife).
- Increase in rates of testicular cancer (lifetime risk of 1%) – evidence linking to environmental exposures

Conclusions

- Substantial evidence exists from laboratory, wildlife, and human studies that environmental exposures can result in a range of chronic diseases in children. Many of these diseases are on the increase.
- Evidence exists of increasing problems in human reproduction – need to pull together trends.
- The causes of infertility are likely multifactorial and it will be difficult in most cases to pinpoint exact causal relations
- We should act on those preventable causes of infertility even when evidence is not conclusive but merely points to a significant problem, particularly when alternatives are available.

Resources

- EPA – America’s Children and the Environment - <http://yosemite.epa.gov/ochp/ochpweb.nsf/content/trends.htm>
- Children’s Health and the Environment: A New Agenda for Prevention Research - <http://ehp.niehs.nih.gov/members/1998/Suppl-3/787-794landrigan/landrigan-full.html>
- In Harms Way - <http://psr.igc.org/ihw-download-report.htm>
- Collaborative on Health and Environment – www.healthandenvironment.org
- Children’s Health and the Environment in North America - http://www.cec.org/files/pdf/POLLUTANTS/CEH-Indicators-fin_en.pdf