

Justice, Environmental Health Laws and Relations Between People

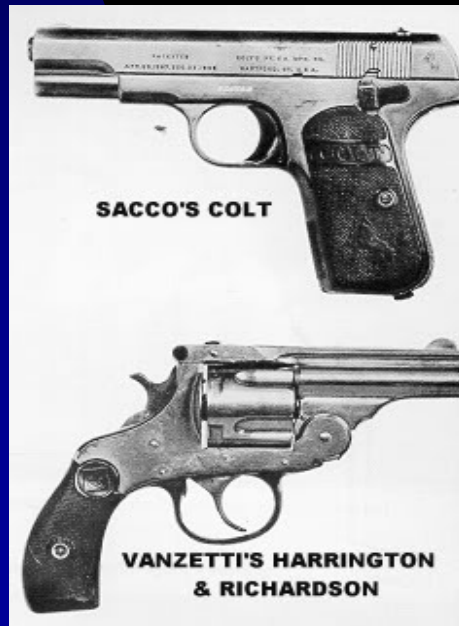
Carl Cranor

Distinguished Professor of Philosophy
Faculty Member, Environmental Toxicology
Graduate Program

University of California
Riverside, CA

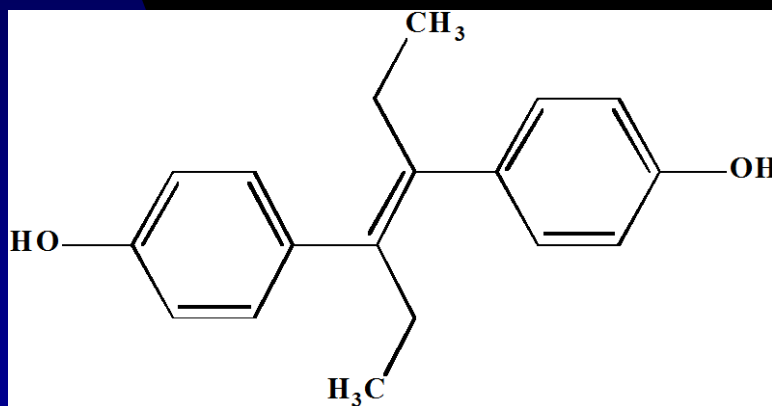
Science And the Law

- Bullets, knives and blunt objects are often philosophers' examples of risk or harm bearing entities.



Using Science And the Law to Protect the Public

- Molecules—**tiny, invisible, undetectable** intruders—can also pose risks or cause harms, but diagnosing their adverse effects is much more subtle and difficult than for the grosser forms of violence. Children are especially susceptible.



Diethylstilbestrol

In utero exposure caused vaginal/cervical cancer at age 20, breast cancer later.

- How can we utilize the law and science to reduce the risks to children from toxic molecules and make the world a safer place?

Generic Legal Strategies to Protect the Public Health

Postmarket laws

Substances enter commerce with *no routine legally required testing or approval* (90-80% of industrial chemicals).

Endocrine disrupter
Screening program

Premarket laws

Pre-mkt *notification law* (TSCA-1979) *No routinely required toxicity data*; only submission of what is known

Pre-mkt *testing and approval laws* *legally require routine toxicity testing & agency approval*, for drugs, pesticides, new food additives (~10-20%).

TOXICOLOGY

The Developmental Basis of Disease

- “*In utero* nutrition and/or *in utero* or neonatal exposures to environmental toxicants **alter susceptibility to disease later in life** [by affecting] the programming of tissue function that occurs during development.” (Heindel, 2008)

The Developmental Basis of Disease

- **Epigenetics:** “These toxicant-induced pathogenic responses are most likely the result of **altered gene expression** or **altered protein regulation** [not a change in the genetic sequence] resulting in altered cell production and cell differentiation . . . ” (Heindel, 2008)
- In turn these “lead to altered [structural] and/or functional character of the tissues, organs and systems” that can lead to diseases, dysfunctions or premature death. (Heindel, 2008)

Recent Science Shows the Inadequacy of Current Laws

- When we add the developmental basis of disease to the known **contamination** of citizens plus humans' **permeability to toxicants** this suggests a problem needing a legal and scientific paradigm change to address adequately.
- We cannot prevent contamination; we need to create legal institutions to **prevent** toxic contamination.

Contamination

- U.S. citizens are contaminated by more than **300 manmade substances** (PFCs, PBDEs, PCBs, organochlorine pesticides, phenols, phthalates, PAHs, and perchlorate); there will be more. Many are known toxicants. (CDC, 2012; Woodruff, et. al., 2011; ACOG, 2013)
- Every pregnant woman is contaminated with at **least 43 substances** (ACOG, 2013), and women's contamination is shared with developing children *in utero*--**the placenta is no significant barrier**. (ACOG, 2013)
- Babies are born with numerous industrial chemicals in their bodies, some toxic. (Fimrite, 2009)

Women's Chemical Burden is Shared with Developing Fetuses and Newborns

- 1965: The womb was seen as a time capsule, **relatively impermeable** to circulating drugs or toxicants. (Needleman & Bellinger, 1994)
- Contradicted by the social catastrophes of **methylmercury** (1960s), **thalidomide** (1960s), and **DES** (1971) showing *in utero* exposures can cause disease.
- Now much more evidence.

Early Catastrophes from *in utero* Contamination: Methylmercury (1950s)



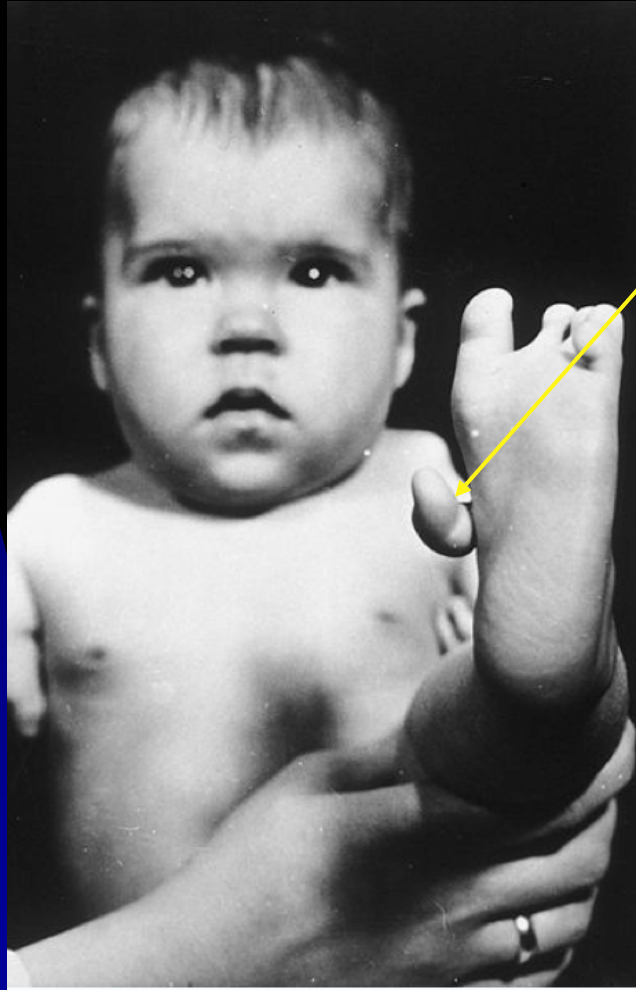
Methylmercury exposure *in utero* at Minimata, Japan, induced **cerebral palsy** as well as

- mental retardation
 - limb deformities
 - constricted visual field
 - sensory disturbance
 - ataxia (poor muscle control)
 - auditory disturbance
 - disturbance of gait
 - death.
-
- Cats having eaten contaminated fish “**danced**” strangely, jumped into the sea; birds **fell from the sky**. (Harada, 1995)

Sandra Bullock signs an autograph for Lisa Patrick, who suffers from **Cerebral Palsy**, and greets fans while at a red carpet premiere of her latest film, "The Blind Side," in [New Orleans](#), Thursday, Nov. 19, 2009. AP Photo

Early Catastrophes from *in utero* Contamination: **Thalidomide** (1960s)

Malformed right limb →



Extra appendage on left foot

Thalidomide induced

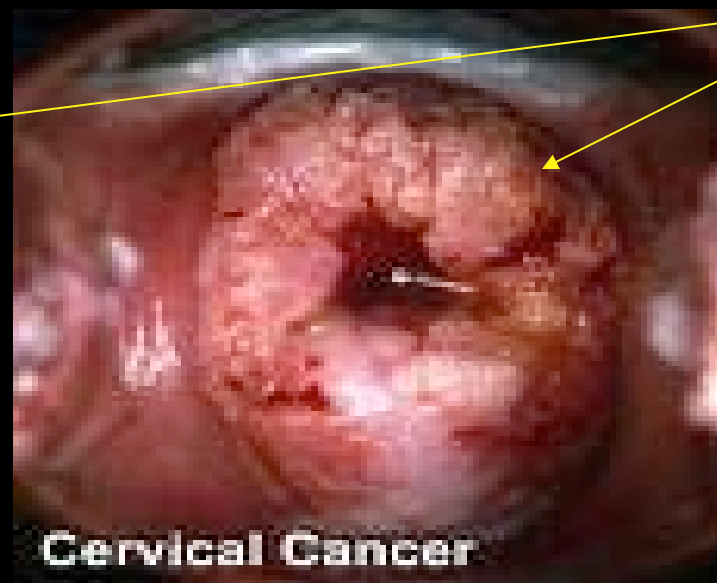
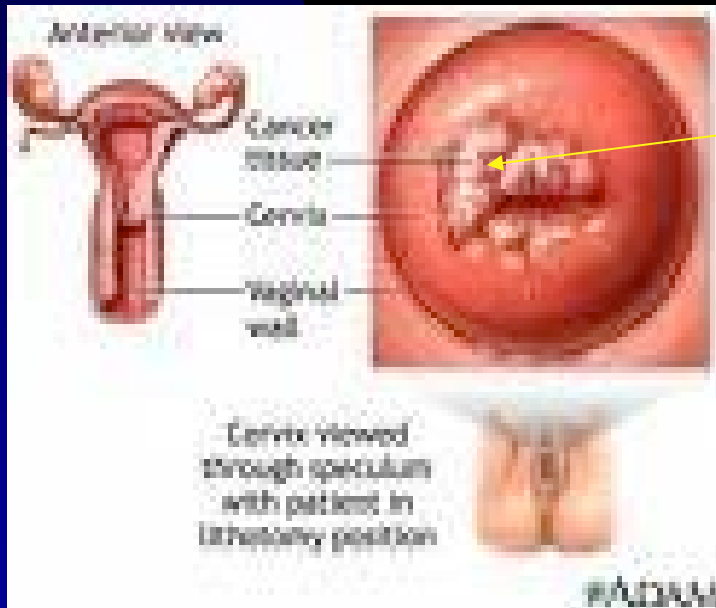
- shortened limbs
- no ears, deafness [subsequent retardation]
- no or small eyeballs
- spinal malformations
- congenital heart disease
- kidney abnormalities
- obstetrical problems (e.g., double vaginas)
- central nervous system problems, but often normal mentality
- autism (30 x higher)
- epilepsy, learning disorders
- death.

National Cancer Institute, 1962

Early Catastrophes from *in utero* Contamination

Diethylstilbestrol (DES) induced **cervical/vaginal cancer** in daughters about 20 years after exposure; 20 years later they were at increased risk of **breast cancer**.

DES mothers were also at **increased risk of breast cancer**.



Cancerous growth

Source: Cedars Sinai Hospital,
<http://www.righthealth.com/Health/Photos%20Of%20Cervical%20Cancer-s?lid=goog-ads-sb-8536643334>

Women's Chemical Burden is Shared with Developing Fetuses and Newborns

- There is “no placental barrier per se: the **vast majority of chemicals** given the pregnant animal (or woman) **reach the fetus in significant concentrations** soon after administration.” (Schardein, 2002)
- New technologies pose problems: **Plastic nanoparticles** can move from mom to baby **through placenta**. (29 March 2010, EHN.org)

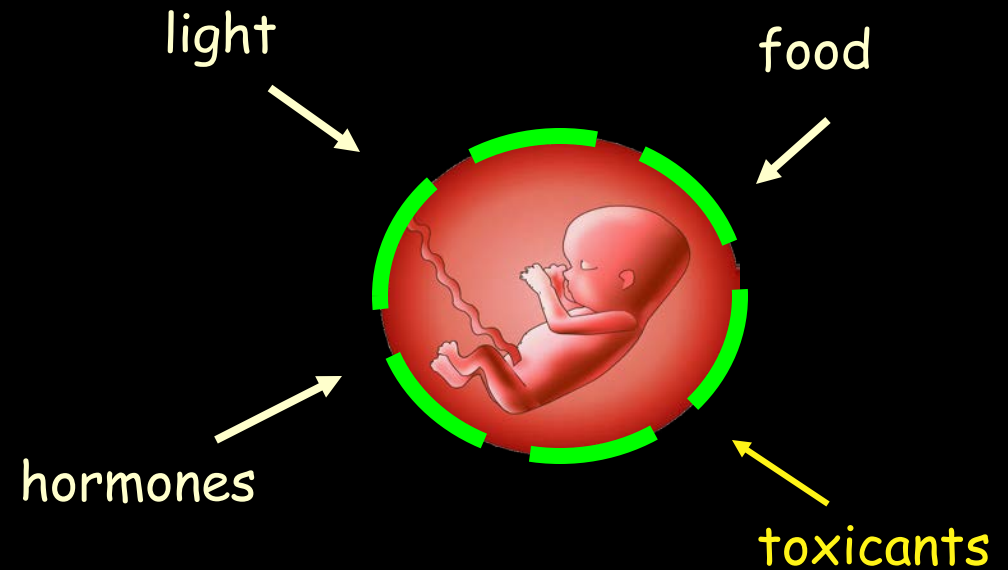
Development is a genetic program

1960s:
Perceived as
comparatively
impermeable (Needleman
And Bellinger, 1995)



Mother is the fetal incubator

Development is an open system (developmental plasticity, ECO-DEVO)



Mother is the fetal environment

Courtesy
Ana Soto

Developing Children Have Greater Exposures

- They can be *exposed to larger doses of toxicants relative to the body weight* than the mother, via cord blood and breast milk. (Faroe's Statement, 2007)
 - Mercury concentrations can be at least 5 times higher in fetal brain than in mother's blood. (Honda, et. al., 2006)
 - Lipophilic substances can be concentrated in cord blood and breast milk (PCBs up to 100 times greater). (Heinzow, et. al., 2007)

Developing Children Have Greater Exposures

- They can be **exposed to *larger doses of toxicants relative to the body weight*** than the mother, via cord blood and breast milk. (Faroe's Statement, 2007)
 - Lead is mobilized as part of the “calcium stream” in pregnant women. (Bellinger & Needleman, 1994)
 - Fetuses have “universal exposure” to BPA, and free BPA (more harmful) has been found in higher concentrations in fetal livers than in maternal blood or urine. (Gerona, et. al., 2013; Nahar, et. al., 2013)

Developing Children Have Greater Exposures

Once born children have

- **Higher metabolism, breathing, absorption, circulation rates.** (Miller, et. al.)
- **Higher fluid and food intake** rates per body weight.
(Miller, et. al.)
- They play close to ground/floor, “mouth” everything, ingest more dust.

Developing Children Are More Susceptible

- In general, they “tend to be **more sensitive** to adverse environmental influences. . . [with] tissues undergoing **rapid cell division**, and [having] much less capacity to metabolize **[and detoxify]** xenobiotics than [do adults].” (Hood, 2006)
- They have **lesser defenses** compared with adults--less developed immune system, blood brain barrier, liver, **detoxifying enzymes**. (Grandjean & Landrigan, 2006; Dietert & Piepenbrink, 2006; Dietert, et. al., 2010)

Developing Children Are More Susceptible

- E.g., the **developing brain** has windows of “unique susceptibility,” unlike adult brains—It must grow from a single cell into billions following “precise pathways” in the “correct sequence” to function properly.

(Grandjean & Landrigan, 2006; Grandjean, 2013)

- The **immune system** is similarly susceptible; for both systems there seems to be “one chance to get it right.”

(Dietert & Zelikoff, 2010)

Summary: Developing Children

- Have greater exposures.
- Are more susceptible to toxicants.
- Have lesser defenses.
- Have a longer lifespan for diseases to develop.

Genetic Variation Increases the Vulnerability

- Some children are more susceptible to
 - **Polycyclic aromatic hydrocarbons.** (Perera, et. al; Uderer, 2014.)
 - **Organophosphate pesticides.** (Eskenazi, et. al., 2008)
 - **Methylmercury.** (Jules, et. al., 2013)

Independent Additive Effects Can Increase Vulnerability

- Substances can affect different “upstream” pathways producing jointly additive effects, but not affecting the same cellular receptors:
 - Dioxin-like PCBs, non-dioxin-like PCBs, perchlorate, and brominated fire retardants (PBDEs), each operating by different pathways can reduce thyroid concentrations in pregnant women, potentially creating neurological risks to fetuses. (Woodruff, Zeise, et. al., 2008)
 - Similar generalized additive effects can adversely affect the immune system.

Exquisite Sensitivity: Tiny Doses Can Pose Problems

- **Lead**—“Exposure to moderate levels of lead during childhood can permanently change important brain chemical levels later in life . . . [contributing to] lower IQs, **violent behavior**, motor skill problems and attention disorders [ADHD]” and cardiovascular disease.

(Cecil, *et. al.*, 4/18/11; Chen & Wessler, 2011; Silbergeld and Rothenberg, 2007)

- There appears to be **no threshold** for lead toxicity during development, early childhood, or even adulthood.

(Lanphear, 2000, Canfield, 2003; Bellinger & Needleman 2003, Goyer & Clarkson, 2006; Weaver & Silbergeld, 2007)

Exquisite Sensitivity: Tiny Doses Can Pose Problems

- **Mutagenic carcinogens**—appear to have **no threshold** for toxicity during development, early childhood, or even adulthood. (David Eastmond, UCR Environmental Toxicology)
- In this, they resemble radiation.

Exquisite Sensitivity: Tiny Doses Can Pose Problems

- For at least one thalidomide baby a single dose of one 50 mg or 100 mg pill caused malformations.
(Claudio, et. al., 2000)
- A single dose of valproic acid (anti-epileptic drug) in animal studies can cause autism-like behavior.
(Dufour-Rainfray, et. al., 2011).

Exquisite Sensitivity: Tiny Doses Can Pose Problems

- A single dose of DES (and some other synthetic estrogens) is sufficient to cause obesity in mice.
(Vom Saal, 2011)

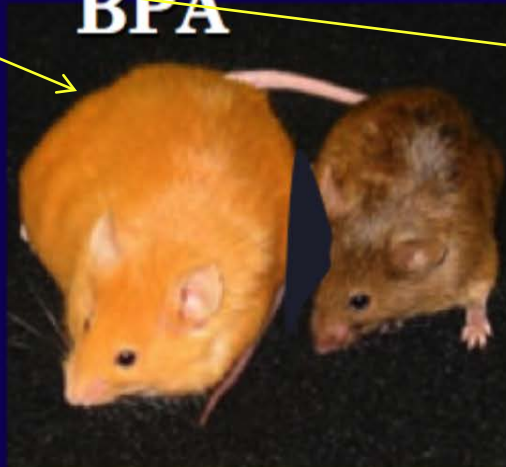
Obese Mouse; Normal Mouse

One gene
methylated *in*
utero at one
location (8ppb)

Same genes,
same diet, same
exercise, different
in utero
exposures to
synthetic
estrogens.

Developmental exposure to BPA or DES Results in Adult Obesity

BPA



Dolinoy, DC, Weidman, JR and Jirtle, RL (2007). Epigenetic gene regulation: linking early developmental environment to adult disease. *Reprod Toxicol* 23:297-307.

DES



Newbold, RR, Padilla-Banks, E, Snyder, RJ and Jefferson, WN (2005). Developmental exposure to estrogenic compounds and obesity. *Birth Defects Res A Clin Mol Teratol* 73:478-80.

Pictures
sent by
Fred
VomSaal

Obese Mouse; Normal Mouse

<http://thehealthyskeptic.org/warning-drinking-bottled-water-could-make-you-fat>

One gene
methylated *in utero*
at one location (8ppb)



Same genome,
same diet,
same exercise,
different *in utero*
exposures to
synthetic estrogens



Tiny Doses Can Pose Problems

- Extremely low doses may sometimes cause greater harm than larger doses.
- High doses of tamoxifen **inhibit** growth of breast cancer cells, lower concentrations **stimulate** breast cancer cell growth, and highest doses are **acutely toxic**. (Vandenberg, 2012)

Worse Effects in Children v. Adults at Same Dose

- **Radiation** and **DDT**: Teenage exposures much worse than adult exposures [human data]. (NAS 1990; Cohn, 2007).
- **Thalidomide** and **DES** [human data].
- **Several pesticides, DES, BPA** contribute to sperm damage and cancers offspring but not in adults [animal data]. (Skinner, numerous papers)
- Infant exposure to **immunotoxics** results in greater dose-sensitivity, greater severity of effects, wider and different range of effects, greater persistence of effects than adult exposure [animal data]. (Dietert, Piepenbrink, 2006)

“Bad Daddy” Factors

(Anthes, *Miller-McCune*, 2010)

- **Toxic contamination of males** with chemotherapeutic agents, lead, mercury, pesticides, solvents can lead to:
 - Degradation of sperm quality; miscarriages; childhood leukemia; birth defects; childhood cancer. (Anthes, *Miller-McCune*, 2010)

“Bad Daddy” Factors

(Anthes, *Miller-McCune*, 2010)

- Toxic contamination of males with **Paxil, anesthetic gases, and morphine** can lead to:
 - Sperm fragmentation; miscarriages; chronic late blooming, abnormal, underweight offspring; still births.

The **Timing** of Exposures and **Transgenerational** Effects

- *SOME ILL-TIMED EXPOSURES DURING DEVELOPMENT OF REPRODUCTIVE ORGANS CAN CAUSE **TRANSGENERATIONAL HARMS**.*
- ***TRANSIENT** CHEMICAL EXPOSURES CAN BECOME **BIOLOGICALLY EMBEDDED** IN INDIVIDUALS, IN THEIR CHILDREN OR GRANDCHILDREN (**MULTIGENERATIONAL**), AND, WITH APPROPRIATE TIMING, IN FAMILY LINES IN GREAT GRANDCHILDREN AND BEYOND (**TRANSGENERATIONAL**).*

Evidentiary Picture

The evidentiary picture for the developmental basis of disease is something like a pointillist painting: parts of the picture filled with numerous data points, others partially filled, some blank, but the general background reasonably solid.



The end result is of considerable concern for children.

A Sunday Afternoon on the Island of La Grande Jatte, Georges Seurat

What Should Be Done?

Legal Failures

The U.S. legal system regulates the **vast majority** (80-90%) of chemical substances with **postmarket** laws: products are

- Permitted into commerce without any **legally required routine premarket testing** under the Toxic Substances Control Act.
- And, remain in commerce until a public health agency
 - bears a legal and scientific burden of proof sufficiently strong to change the status quo to reduce exposures or remove them .
- Typically an agency must show that they pose **risks of harm** or actually **cause harm**.

Legal Failures

Postmarket laws

- Encourage **willful** toxic **ignorance**. For 80% to 90% of new industrial chemicals there is **no or little knowledge about whether they are toxic or not**.
- **Create barriers to better health protections**. Reducing toxic risks is so difficult improved health protections become slothfully mired in procrastination, obfuscation, and endless disputes--TCE (**20+** years), dioxin (**20+**), perchloroethylene (**13+**), formaldehyde (**11+**), naphthalene (**9+**) (GAO, 2005).
- Make **haphazard guinea pigs** of adults and children alike, increasing risks.

Legal Failures

Premarket testing and approval laws (e.g., for drugs and pesticides) are not free from critique but much better:

- Some developmental effects of pharmaceuticals and pesticides have been missed.
- These will also need improvement.

JUSTICE

Given the Developmental Origins of Disease Existing Laws Are Unjust

- Postmarket laws **do not prevent** and **cannot prevent** children and adults from diseases that can be induced by toxic substances during development.
- These are injustices resulting from the actions of fellow citizens; they do not “just happen to us” as do naturally occurring diseases, e.g., measles or mumps.

Given the Developmental Origins of Disease Existing Laws Are Unjust

- Such laws subject citizens
 - To legal “**battery**” (from untested substances),
 - To actual **harm**,
 - To loss of **fair equality of opportunities over a lifetime**, and
 - In many cases to **substantial loss of income and wealth**. (Prosser and Keaton on

Torts, 1984; John Rawls, *A Theory of Justice*, and Norman Daniels “Just Health Care” 1984).

Public Health Officials Successfully Prevented Diseases Earlier in Our History

- Diseases were prevented by chlorinating drinking water, cleaning up sewage, and discovering vaccines for diseases.
- Such solutions are not available for diseases caused by toxic exposures triggered by the products of fellow citizens.
- We need legal changes to prevent unjust distributions of disease.

Juxtapose the Ethics of Medical Experiments with Exposures to Industrial Compounds

- Medical experiments require, *inter alia*:
 - Informed consent by participants, freedom to leave experiments at any time, special/central concern for participants, and defeasible prohibitions against experiments on children.
 - **Special concern for children**; testing of children only if no other way to obtain data to benefit children and concern for the experimental subject is central.
 - **Reasonable assurances of safety** for participants.
 - **Independent scientific and ethical** review of the experiment and its provisions.

Cognitive Dissonance: The Ethics of Medical Testing Suggests Citizens Are Treated as Haphazard Guinea Pigs

Ethical constraints on medical testing reveal **shortcomings** of laws that permit contamination of citizens without toxicity data:

- No prior preparations and reasonable assurances of safety.*
- No careful assessment of safe exposures.*
- No special concern for children.*
- Concern for contaminated person is not central.*
- No independent scientific or ethical oversight.*
- Without these protections invasions resemble **battery/trespass**.

Battery

- Exposure to untested substances without one's knowledge constitutes battery: A knowingly causes contact with B that B **reasonably regards** as **offensive**.
- “Battery [a foundational legal cause of action] protects **bodily integrity** and **individual autonomy**, creating the essential status and space for social interactions. Indeed, proscribing harmful or offensive physical contacts is a structural prerequisite for a functional society.” [Provides a legal outlet to reduce violence].
(Mary Lyndon, “The Toxicity of Low Dose Chemical Exposures,” 2011)

Battery

- “A contact which causes no bodily harm may be actionable as a violation of a right to freedom from intentional infliction of offensive bodily contacts.” (Restatement of Torts, 3d)
- “If it is tortious to seriously insult or startle someone, it would seem an even greater transgression of social boundaries to inflict a silent, invisible bodily contact with a possible toxicant, leaving those ‘touched’ to await whatever may come.” (Lyndon, 2011)

Battery

- The person who is concerned about exposure may react with anxiety, fear, and anger, dismay and helplessness. ... [T]he sociological literature [on] how ordinary people experience the prospect of dangers ... report[s] that substantial individual and community damage results.” (Lyndon, 2011)
- Exposure of pregnant women to DES without their knowledge constitutes battery. (Mink v. U. of Chicago)

Justice

- Two types of injustice:
 - Both battery from **untested** substances and actual **harm** from **toxic substances** constitute “assaults” against the person—a violation of an equal liberties principle of justice. (John Rawls, *A Theory of Justice*, 1971)

Justice

- Third, if harm from a toxic exposure is **sufficient to interfere with normal biological functioning** over a **longer period of time**, e.g., chronic diseases, cancer, neurological deficits, immunological adversity, reproductive problems, so that these reduce a person's normal opportunity range in the society, it constitutes a violation of **fair equality of opportunity**. (Normal Daniels, Distributive Justice and Just Health-care," 1984)

Justice

Finally, if exposures to toxic substances **cause harm** or the threat of exposures **causes negative externalities** for other citizens, who take precautionary actions to avoid toxicants, this constitutes a violation of a **just distribution of income and wealth** compared to a circumstance in which such externalities are not present. (Rawls, *A Theory of Justice*)

- Negative externalities are social costs of activities that are not incorporated into the market prices of those activities.

Justice

- **Diseases are expensive:** \$76.6 billion in 2008 alone for the portion of diseases attributable to lead poisoning, childhood cancer, asthma, intellectual disability, autism, attention deficit disorder (3.5% of all healthcare costs) . (Trasande and Liu, *Health Affairs*, May 4, 2011).
- Such economic distributive consequences very likely exacerbate income and wealth **inequalities**.

Generic Legal Strategies for Public Health Protections

Postmarket laws

Substances enter commerce with *no required testing or approval* (90- 80% of industrial chemicals)

Premarket laws

Premarkt *notification* laws (1979)
No required testing; only submission of what is known

Premarkt *testing and approval* laws
require routine testing & agency approval, for drugs, pesticides, new food additives (~*10-20%*).

Endocrine disrupter
Screening program

Legal Failures

Some laws governing toxic molecules were inspired by nuisance laws:

- Typical nuisances: vibration, blasting, destruction of crops, pollution of a stream, smoke, dust, unpleasant odors, excessive light, loud noises, repeated and annoying phone calls. They are offensive or inconvenient.
- These are quite unlike **molecular invaders** that are tiny, invisible, silent, otherwise undetectable.

Legal Failures

Nuisances

- Are readily perceptible.
 - Announce their presence.
 - Immediately disturb one's space.
 - Have obvious causal effects.
-
- All facilitate postmarket legal actions.

Molecules

- Are **not**.
 - Do **not**.
 - Do **not**.
 - Typically **do not** have immediate effects.
-
- Postmarket laws poorly control them.

Further Diagnosis of Legal Failures

Criminal Law v. Premarket Testing Laws

Criminal Law (Inherent protection)

The criminal law **prevents willful ignorance** about crimes with its responsibility and excusing conditions.

Once an offender is arrested the crime and harm typically ceases.

Premarket Laws (Inherent protection)

Premarket laws require toxicity testing of products & independent scientific review of the tests before marketing.

Testing creates **practical discouragement** of willful ignorance about risky products—testing *per force* **creates information** about risks. Scientific review catches other risks.

Risks and harm continue with product in the market; publicity, doctors, & pharmacists can alert consumers to risks (esp. for pharmaceuticals).

Deeper Problems with Postmarket Laws: How Citizens Are Treated

Criminal Law (Metaphysics & Epistemology)

Humans, **largish**, **perceptible** physical objects, commit crimes and typically leave behind **detectable physical traces**.

This assists self-protection & assists others in identifying criminals.

This assists evidence gathering (from residual traces of the crime).

Consider: traces from bombings, murders, thefts, rapes, and so on. But not always true.

Premarket Laws (Metaphysics & Epistemology)

Harm bearers are molecules—**tiny** and **undetectable** (invisible, silent), unavailable to our senses; no or few residual traces of harm.

These features **undermine self-protection** and others identifying toxic molecules (premarket testing compensates).

They also undermine **evidence gathering** (from residual traces of cause of harm), but again premarket testing compensates.

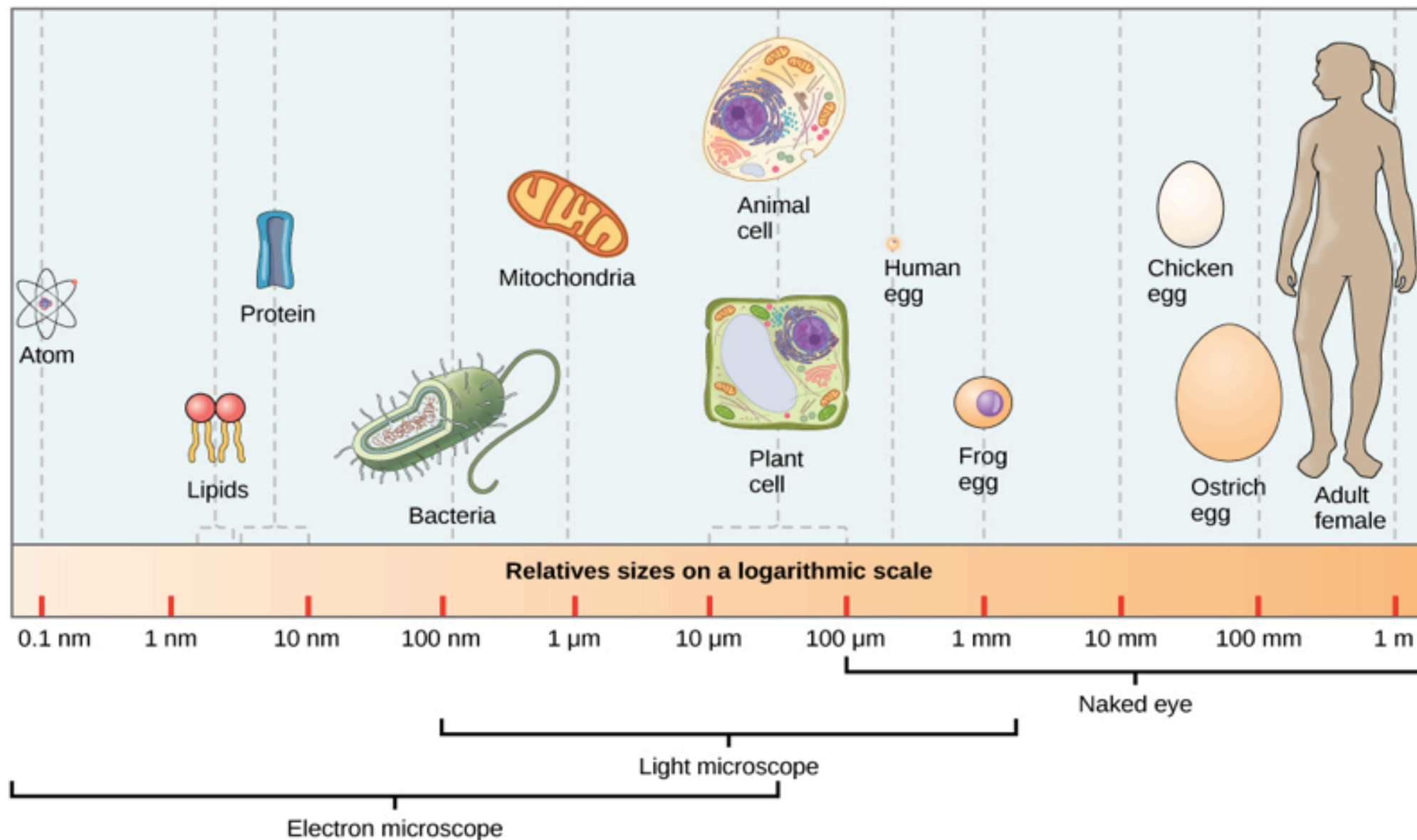


Figure 2: This figure shows the relative sizes of different kinds of cells and cellular components. An adult human is shown for comparison.

Premarket Testing Laws v. TSCA Provisions and Postmarket Laws

Premarket Laws (Inherent protection)

Premarket laws protect the public by requiring toxicity testing of products & independent scientific review of the tests before marketing.

These create **practical barriers** to willful ignorance about risky products—Testing *per force* **creates awareness** of many risks with information about risks. Scientific review catches other risks.

Risks & harm continue with product in the market; publicity, doctors & pharmacists can alert consumers to risks (esp. for drugs).

Postmarket Laws (Inherent protection)

TSCA: no routine toxicity testing of products before exposures (With burdensome procedures EPA can order testing).

Companies easily can **know nothing** about their products' risks. Very weak independent scientific review by EPA—structure-activity data guide the effort.

TSCA **invites willful ignorance** about products—avoidance and competitive incentives; firms have eliminated toxicology departments.

Risks disperse widely; publicity likely a poor alert for consumers. These continue until there is no exposure—especially long for persistent chemicals.

Premarket Testing Laws v. TSCA Provisions and Postmarket Laws

Premarket Laws (self-protection)

Molecules are bearers of harm—tiny, invisible and undetectable; premarket testing compensates.

Drugs: physicians, pharmacists, labels & the FDA's adverse event reporting system substantially aid protections.

Pesticides: pesticide applicators, EPA's reporting system, and labels provide some protections.

Others cannot witness harms or do anything to provide evidence of violations.

Postmarket Laws (self-protection)

Molecules are bearers of harm—tiny , invisible and undetectable; no premarket testing to compensate.

No analogues of physicians/pharmacists/pesticide applicators; no labels; poor adverse event reporting.

Others cannot witness harms or do anything to provide evidence of violations.

The Law Must Compensate to Better Protect Citizens from Molecules

- Because of differences between typical bearers of crimes and molecular bearers of harm, the law must
 - **Identify** sources of harm—no or few clues for citizens.
 - Ensure as best it can the **safety** of molecular exposures—“police” & citizens cannot “see” or “detect” them; citizens cannot create “safeguards” against them and can do little to protect themselves.

The Law Must Compensate to Better Protect Citizens from Molecules

- Because “catching” harmful molecules (v. catching criminals) is so difficult after harm is done, the law has to better ensure safety upfront.
- Molecular harms are like serial criminals, not one-off events—and much harder to “catch.”
- Social influences cannot modify the behavior of harm bearers and often seem to have little effect on company decision makers.

What Should Be Done?

- Both pesticides and industrial chemicals can be ingested, inhaled, or absorbed through the skin.
- The pesticide laws seek to protect us from these sources of contamination; we need the same protections from industrial chemicals.

Some Conclusions

- Molecular contamination is inevitable, unavoidable; there is no place to hide.
- Contamination by **toxic** molecules is the problem.
- Current laws permit **toxic contamination**, **willful ignorance** of toxicity, **slothful reduction of risks** and **little prevention** of environmentally induced diseases.
- We need to move to a variation of premarket testing for toxicity to achieve these goals.



Thank you

Early Immune System Dysfunctions May Signal Life-long Problems

Immune system patterns: **Allergy**-related; **autoimmune**-related

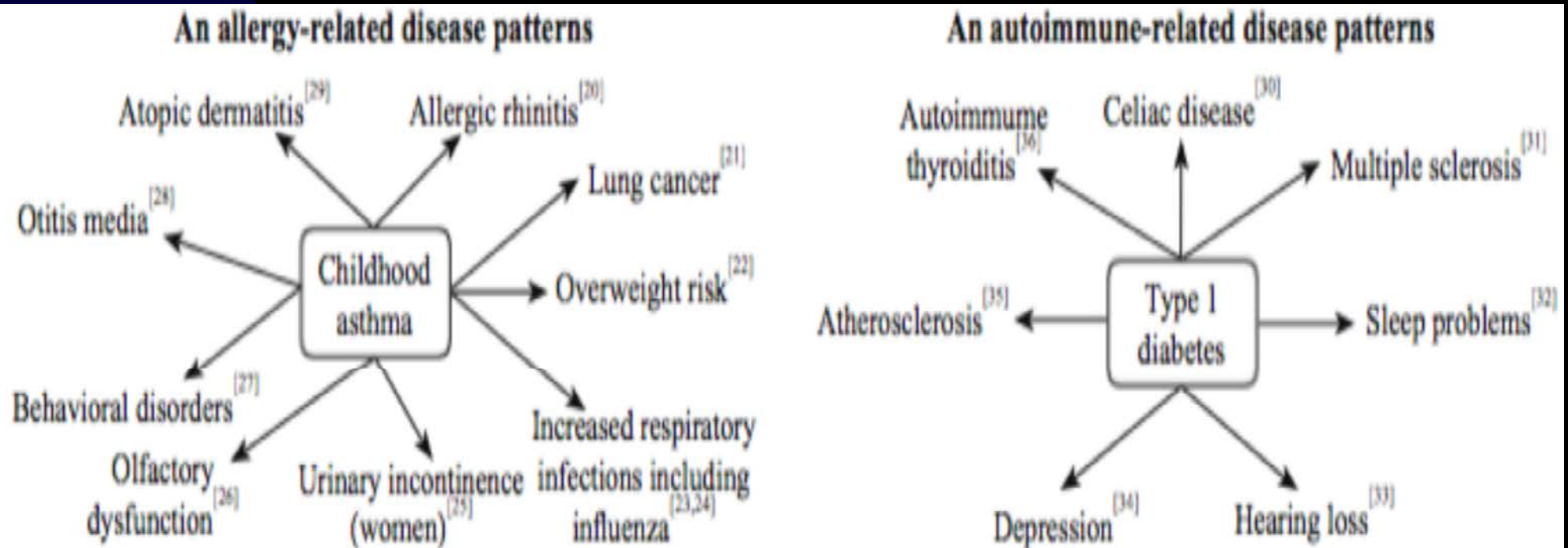
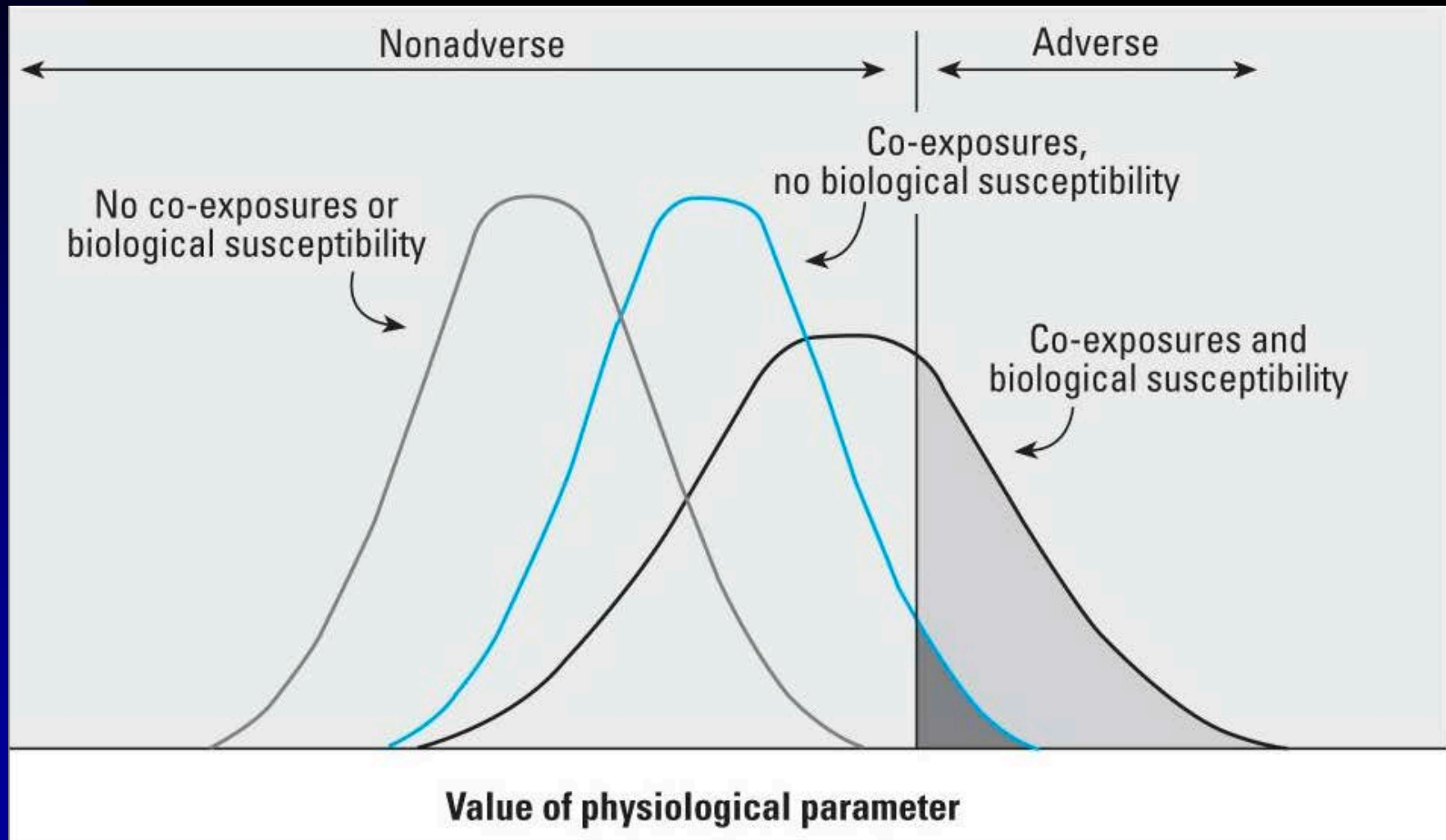
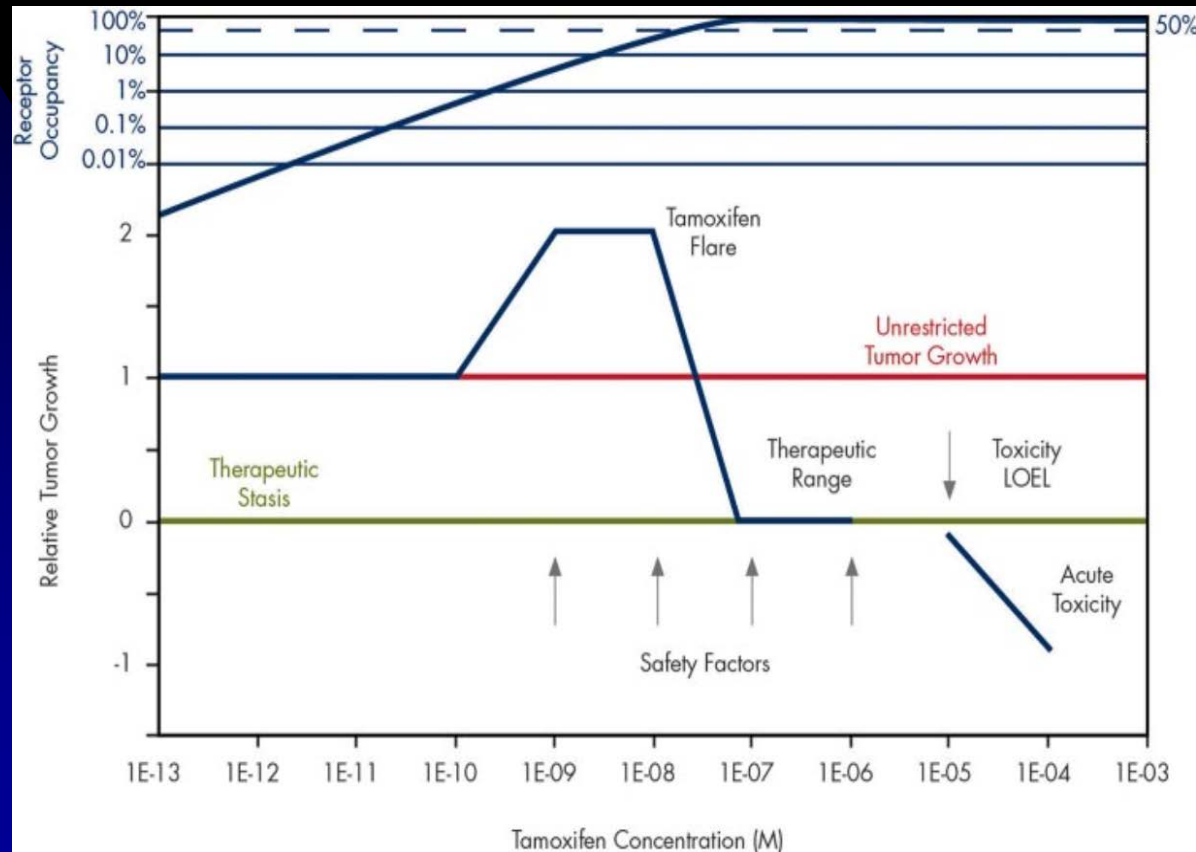


Fig. 1. Two examples of patterns of immune-related diseases. Both an allergy-related example (left) and an autoimmune-related example (right) are presented. The primary pediatric-onset immune-related disease is indicated in the center of each pattern. Secondary diseases and conditions that may arise either simultaneously or later in life and are connected to the primary disease by elevated risk are shown via arrows.

Additive effects and Susceptibility Together Increase Vulnerability



Low, Even Tiny, Doses May be Worse Than Large Doses



Dose-response ranges for tamoxifen
in breast cancer therapy (Vandenberg, 2012)

The **Timing** of Exposures and **Transgenerational** Effects

- **E.g. Cancer plus reproductive effects on germ cells:**
 - Exposure of male rats during reproductive organ development to **some pesticides** and **bisphenol A** (individually) causes sperm damage, sterility, prostate disease, kidney disease, immune system abnormalities, testis abnormalities, and tumor development (e.g. breast). (Manikkam, et. al. 2012)
 - Analogous results were seen in female rats exposed in utero-- polycystic ovarian disease (infrequent ovulation, multiple persistent ovarian cysts [seen in 6-18% women], and primary ovarian insufficiency (POI). (Nilsson, et al., Skinner, 2012)
 - The effects persisted through 4 generations, making them **transgenerational**. (Anway, et al., 2006; Skinner, et. al., 2007, 2009; Manikkam, et. al. 2012)

Comparison with the Ethics of Medical Testing Suggests Further Issues

Existing chemical laws suggest the following points about exposures to industrial chemicals:

- Citizens do not morally warrant prior preparations, reasonable assurances of safety, or careful assessments of safe exposures.*
- Children do not morally warrant special concern, despite their special susceptibilities.*
- The certain contamination of others person is not of central concern.*
- The issues at stake morally warrant no independent scientific or ethical oversight.*

What Should Be Done?

Premarket Testing is Efficient

- **Diseases are expensive:** \$76.6 billion in 2008 alone for the portion of diseases attributable to lead poisoning, childhood cancer, asthma, intellectual disability, autism, attention deficit disorder (3.5% of all healthcare costs) . (Trasande and Liu, *Health Affairs*, May 4, 2011).
- **Toxicity testing is efficient:** The 11-year cost to test and review 30,000 chemicals under REACH is about \$5 billion, or less than 1 euro per European citizen per year for 11 years. (Ackerman, 2006)
- Premarket testing to reduce adverse health effects would be a bargain at two or three times that amount.