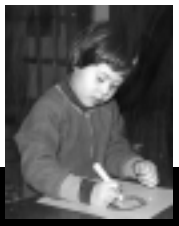


Executive Summary

This report examines the contribution of toxic chemicals to neurodevelopmental, learning, and behavioral disabilities in children. These disabilities are clearly the result of complex interactions among genetic, environmental and social factors that impact children during vulnerable periods of development. Toxic exposures deserve special scrutiny because they are *preventable* causes of harm.

Toxic exposures deserve special scrutiny because they are preventable causes of harm.

1. An epidemic of developmental, learning, and behavioral disabilities has become evident among children.

- It is estimated that nearly 12 million children (17%) in the United States under age 18 suffer from one or more learning, developmental, or behavioral disabilities.
- Attention deficit hyperactivity disorder (ADHD), according to conservative estimates, affects 3 to 6% of all school children, though recent evidence suggests the prevalence may be as high as 17%. The number of children taking the drug Ritalin for this disorder has roughly doubled every 4-7 years since 1971 to reach its current estimate of about 1.5 million.
- Learning disabilities alone may affect approximately 5-10% of children in public schools.
- The number of children in special education programs classified with learning disabilities increased 191% from 1977-1994.
- Approximately 1% of all children are mentally retarded.
- The incidence of autism may be as high as 2 per 1000 children. One study of autism prevalence between 1966 and 1997 showed a doubling of rates over that time frame. Within the state of California, the number of children entered into the autism registry increased by 210% between 1987 and 1998.

These trends may reflect true increases, improved detection, reporting or record keeping, or some combination of these factors. Whether new or newly recognized, these statistics suggest a problem of epidemic proportion.

2. Animal and human studies demonstrate that a variety of chemicals commonly encountered in industry and the home can contribute to developmental, learning, and behavioral disabilities.

Developmental neurotoxicants are chemicals that are toxic to the developing brain. They include the metals lead, mercury, cadmium, and manganese; nicotine; pesticides such as organophosphates and others that are widely used in homes and schools; dioxin and PCBs that bioaccumulate in the food chain; and solvents, including ethanol and others used in paints, glues and cleaning solutions. These chemicals may be directly toxic to cells or interfere with hormones (endocrine disruptors), neurotransmitters, or other growth factors.

Lead

- Increases in blood lead levels during infancy and childhood are associated with attention deficits, increased impulsiveness, reduced school performance, aggression, and delinquent behavior.
- Effects on learning are seen at blood lead levels below those currently considered "safe."

Mercury

- Large fetal exposures to methylmercury cause mental retardation, gait and visual disturbances.
- Smaller fetal exposures, such as those resulting from regular maternal fish consumption, have been implicated in language, attention, and memory impairments that appear to be permanent.

Manganese

- Unlike many other metals, some manganese is essential as a catalyst in several critically important enzymatic processes. However, several studies report a relationship between excessive childhood levels of manganese exposure and hyperactivity or learning disabilities.

Nicotine

- Children born to women who smoke during pregnancy are at risk for IQ deficits, learning disorders, and attention deficits.
- Children born to women who are passively exposed to cigarette smoke are also at risk for impaired speech, language skills, and intelligence.

Dioxins and PCBs

- Monkeys exposed to dioxin as fetuses show evidence of learning disabilities.
- Humans and animals exposed to low levels of PCBs as fetuses have learning disabilities.
- Children exposed to PCBs during fetal life show IQ deficits, hyperactivity, and attention deficits when tested years later.

Pesticides

- Animal tests of pesticides belonging to the commonly-used organophosphate class of chemicals show that small single doses on a critical day of development can cause hyperactivity and permanent changes in neurotransmitter receptor levels in the brain.
- One of the most commonly used organophosphates, chlorpyrifos (Dursban), decreases DNA synthesis in the developing brain, resulting in deficits in cell numbers.
- Some pyrethroids, another commonly used class of pesticides, also cause permanent hyperactivity in animals exposed to small doses on a single critical day of development.
- Children exposed to a variety of pesticides in an agricultural community in Mexico show impaired stamina, coordination, memory, and capacity to represent familiar subjects in drawings.

Solvents

- Exposure to organic solvents during development may cause a spectrum of disorders including structural birth defects, hyperactivity, attention deficits, reduced IQ, learning and memory deficiencies.
- As little as one alcoholic drink a day by a mother during pregnancy may cause her offspring to exhibit impulsive behavior and lasting deficits in memory, IQ, school performance, and social adaptability.
- Animal and limited human studies show that exposures to common chemicals like toluene, trichloroethylene, xylene, and styrene during pregnancy can also cause learning deficiencies and altered behavior in offspring, particularly after fairly large exposures.

3. A deluge of highly technical information has created communication gaps within the field of child development.

- The recent explosion of research in the many sciences related to child development has produced a glut of highly technical information not readily understood by those outside the field in which the research was performed.

Some pyrethroids cause permanent hyperactivity in animals exposed to small doses on a single critical day of development.

- A communication gap has resulted, dividing fields of research and separating the domains of research, clinical practice, and the public.
- Behavior and cognition can be described using clinical disorders, such as ADHD or Asperger's syndrome, which are categorical and qualitative. Alternatively, behavior and cognition can be described using abilities/traits, such as attention and memory, which are continuous and quantitative. Abilities/traits cluster into disorders in various ways and are emerging as an important bridge among the scientific disciplines focusing on child development.

Breast-fed infants are exposed to levels of dioxin that exceed adult exposures by as much as a factor of 50.

4. Although genetic factors are important, they should not be viewed in isolation.

Certain genes may be susceptible to or cause individuals to be more susceptible to environmental "triggers." Particular vulnerability to a chemical exposure may be the result of a single or multiple interacting genes. For example:

- Gene-coding for certain enzymes can influence how chemicals are metabolized or stored in the body, or increase a person's susceptibility to a chemical. For example, a gene coding for the enzyme, delta aminolevulinic acid dehydratase (ALA-D), can influence lead metabolism, bone storage of lead, and blood lead levels.
- Two genes increase susceptibility to organophosphate pesticides. One, carried by 4% of the population, results in lower levels of acetylcholinesterase, the target enzyme of organophosphates. The other, carried by 30-40% of the population, results in reductions in paroxonase, an enzyme that plays an important role in breaking down organophosphate pesticides.
- Antibody reactions to infections is another important gene-environment interaction. For example, studies suggest that "PANDAS" (pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection), that may affect patients with obsessive compulsive disorder, Tourette's syndrome and tics, result from streptococcal antibodies that cross react with critical brain structures in genetically susceptible children.

5. Neurotoxicants are not merely a potential threat to children. In some instances, adverse impacts are seen at current exposure levels.

- According to EPA estimates, about 1.16 million women in the U.S. of childbearing years eat sufficient amounts of mercury-contaminated fish to risk damaging brain development of their children.
- Breast-fed infants are exposed to levels of dioxin that exceed adult exposures by as much as a factor of 50. Dioxin exposures of this magnitude have been shown to cause abnormal social behavior in monkeys exposed before birth through the maternal diet. (While breast milk contaminants may compromise some of the cognitive benefits of breast feeding, breast milk remains strongly preferred over infant formula due to numerous important benefits to infant health.)
- Prenatal exposure to PCBs at ambient environmental levels adversely affects brain development, causing attention and IQ deficits, which remain detectable years later and may be permanent.
- Neurotoxicants that appear to have trivial effects on an individual have profound impacts when applied across populations. For example, a loss of 5 points in IQ is of minimal significance in a person with an average IQ. However a shift of 5 IQ

points in the average IQ of a population of 260 million increases the number of functionally disabled by over 50% (from 6 to 9.4 million), and decreases the number of gifted by over 50% (from 6 to 2.6 million).

6. Vast quantities of neurotoxic chemicals are released into the environment each year.

- Of the top 20 chemicals reported by the Toxics Release Inventory as released in the largest quantities into the environment in 1997, nearly three-quarters are known or suspected neurotoxicants. They include methanol, ammonia, manganese compounds, toluene, phosphoric acid, xylene, n-hexane, chlorine, methyl ethyl ketone, carbon disulfide, dichloromethane, styrene, lead compounds, and glycol ethers. Over a billion pounds of these neurotoxic chemicals were released directly on-site by large, industrial facilities into the air, water, and land.
- Vast quantities of neurotoxic chemicals are also used in industrial processes and incorporated into products. For example, according to 1997 data from the Massachusetts Toxics Use Reduction Act, over half of the top twenty chemicals in use (over 500 million pounds), and half of those incorporated into products in Massachusetts, are known or suspected neurotoxicants.
- Use of lead in manufacturing increased 77% in Massachusetts between 1990-1997.

- An additional 1.2 billion pounds of registered pesticide products are intentionally and legally released each year in the United States.
- Mercury contamination of our waterways is so widespread that 40 states have issued one or more health advisories warning pregnant women or women of reproductive age to avoid or limit fish consumption. Ten states have issued advisories for every lake and river within the state's borders.

7. Environmental releases often lead to human exposures with potential for harm.

Dispersion of these chemicals is global.

- One million children in the US exceed the currently accepted threshold for blood lead level exposure that affects behavior and cognition (10 micrograms/dl). Updating the toxic threshold in keeping with the results of the most

recent studies would further lower this threshold, resulting in the addition of millions children to the roles of those impaired by lead exposure.

- A metabolite of the pesticide chlorpyrifos is present in the urine of over 80% of adults and 90% of children from representative population samples.
- Inuit mothers in the Arctic, far from sources of industrial pollution, have some of the highest levels of PCBs in their breast milk as a result of a diet rich in marine mammal fat.

8. The historical record clearly reveals that our scientific understanding of the effects of toxic exposures is not sufficiently developed to accurately predict the impact of toxicants, and that our regulatory regime has failed to protect children.

a. As testing procedures advance, we learn that lower and lower doses are harmful.

The historical record shows that "safe thresholds" for known neurotoxicants have been continuously revised downward as scientific knowledge advances. For example, the initial "safe" blood lead level was set at 60 micrograms/deciliter (ug/dl) in 1960. This was revised down to 10 ug/dl in 1990. Current studies suggest that lead may have no identifiable exposure level that is "safe." The estimated "toxic threshold" for mercury has also relentlessly fallen, and like lead, any level of exposure may be harmful.

Such results raise serious questions about the adequacy of the current regulatory regime, which, by design, permits children to be exposed up to "toxic thresholds" that rapidly become obsolete.

b. Most chemicals are not tested for their general toxicity in animals or humans, not to mention toxicity to a child's developing brain specifically.

Nearly 75% of the top high production and volume chemicals have undergone little or no toxicity testing. However, the EPA estimates that up to 28% of all chemicals in the current inventory of about 80,000 have neurotoxic potential. In addition:

- Complete tests for developmental neurotoxicity have been submitted to EPA for only 12 chemicals - nine pesticides and three solvents – as of December 1998.
- Testing for developmental neurotoxicity is not required even in the registration or re-registration of pesticides, one of the strictest areas of chemical regulation

c. Even when regulated, the risks from chemical exposure are estimated for one chemical at a time, while children are exposed to many toxicants in complex mixtures throughout development. Multiple chemical exposures often interact to magnify damaging effects or cause new types of harm.

With the exception of pesticides used on the food supply, current regimes regulate only one chemical at a time and do not take into account the potential for interactions. Since real world

exposures are to multiple chemicals, current regulatory standards, based on single chemical exposures, are inherently incapable of providing adequate margins of safety.

- New studies in humans and in the laboratory show that PCBs and mercury interact to cause harm at lower thresholds than either substance acting alone.
- A recent 5-year pesticide study suggests that combinations of commonly used agricultural chemicals, in levels typically found in groundwater, can significantly influence immune and endocrine systems, as well as neurological function, in laboratory animals.

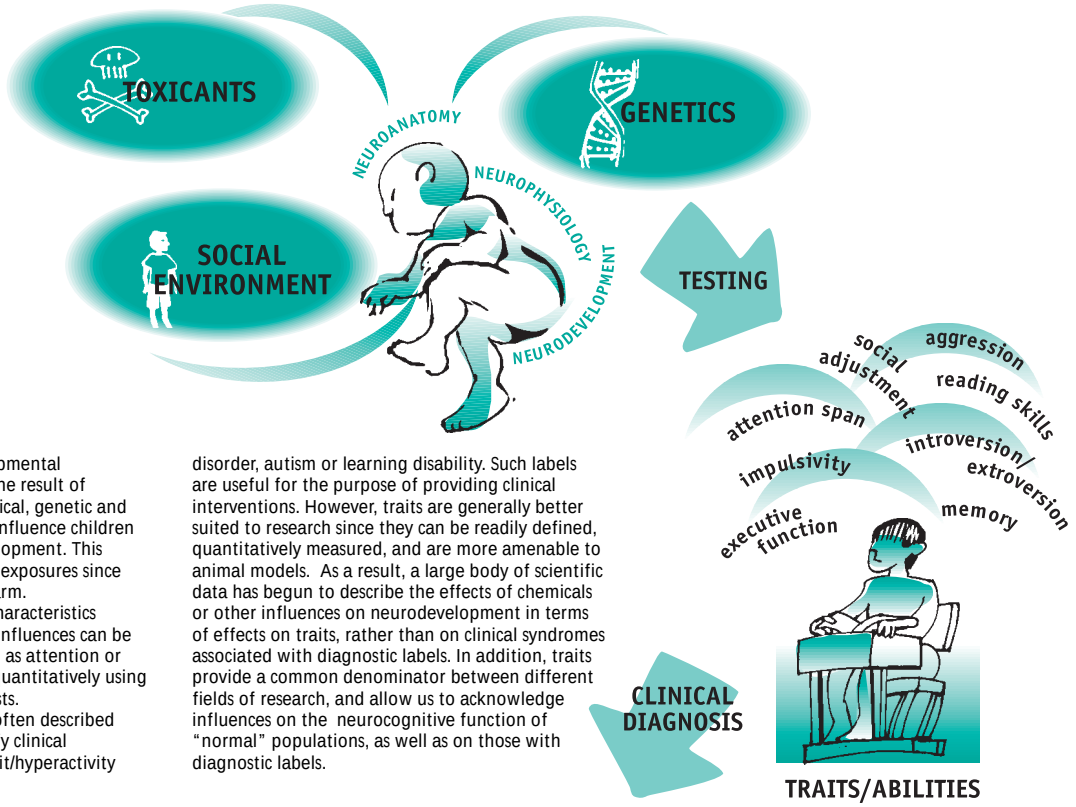
d. Animal studies generally underestimate human vulnerability to neurotoxicants.

- Animal studies of lead, mercury and PCBs each underestimated the levels of exposures that cause effects in humans by 100-10,000-fold.
- Regulatory decisions that rely largely on toxicity testing in genetically similar animals under controlled laboratory conditions will continue to fail to reflect threats to the capacities and complexity of the human brain as well as important gene-environment interactions.

9. Protecting our children from preventable and potentially harmful exposures requires a precautionary policy that can only occur with basic changes in the regulatory process.

- The inability of the current regulatory system to protect public health is not surprising, considering the disproportionate influence of special interests in the regulatory process. When there is evidence for serious, widespread and irreversible harm, as described in this report, residual scientific uncertainties should not be used to delay precautionary actions. Actions should include reduction and or elimination of exposures as well as further scientific investigation of developmental neurotoxicity.

Framework for Understanding



Learning, behavior, and developmental disabilities in children are clearly the result of complex interactions among chemical, genetic and social-environmental factors that influence children during vulnerable periods of development. This report focuses on the role of toxic exposures since they are a preventable cause of harm.

The cognitive and behavioral characteristics that result from these interacting influences can be described as traits or abilities, such as attention or memory, which can be measured quantitatively using a variety of neuropsychological tests.

Aggregates of these traits are often described using diagnostic labels that identify clinical syndromes, such as attention deficit/hyperactivity disorder, autism or learning disability. Such labels are useful for the purpose of providing clinical interventions. However, traits are generally better suited to research since they can be readily defined, quantitatively measured, and are more amenable to animal models. As a result, a large body of scientific data has begun to describe the effects of chemicals or other influences on neurodevelopment in terms of effects on traits, rather than on clinical syndromes associated with diagnostic labels. In addition, traits provide a common denominator between different fields of research, and allow us to acknowledge influences on the neurocognitive function of "normal" populations, as well as on those with diagnostic labels.