

Northwest Hazardous Waste Conference

Toxic Threats to Child Development
April 13, 2004 – 1:00-3:00 pm

**Lessons from Toxicology:
Children's Vulnerability to
Chemical Exposures**



Toxicology Definitions

**The study of poisons
or
the adverse effects of chemical and
physical agents on living
organisms.**



Ancient Awareness

399 BC Death of Socrates by Hemlock

Socrates was charged with religious heresy and corrupting the morals of local youth.

The active chemical used was the alkaloid coniine which, when ingested causes paralysis, convulsions and potentially death.



Environmental Health

“Conditions that ensure that all living things have the best opportunity to reach and maintain their full genetic potential.”

Steven G. Gilbert, 1999



What do these have in common?

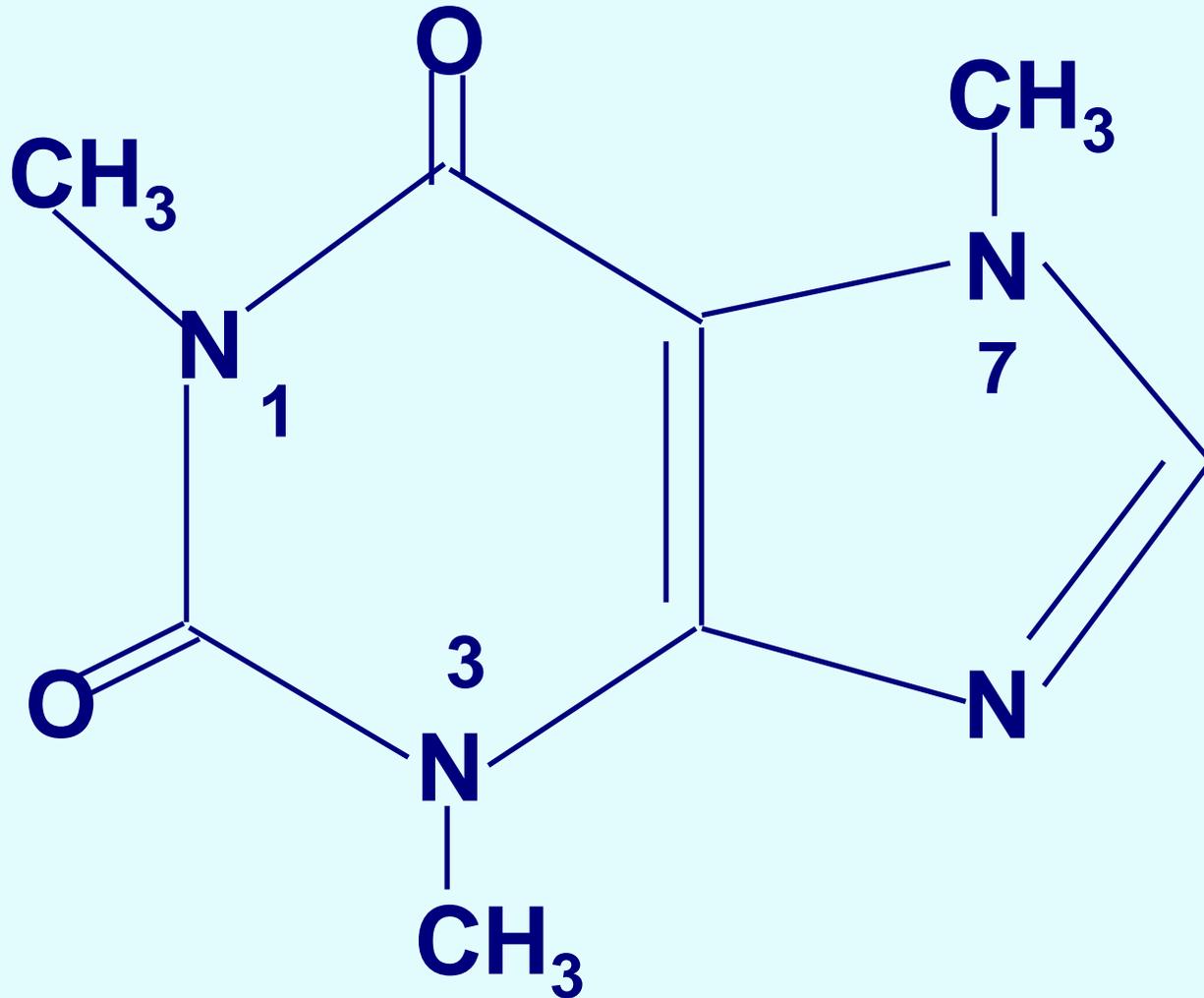
- **Hong Kong**
- **Princess Diana**
- **Ambassador to Mexico**
- **Coeur d'Alene, Silver Valley, ID**
- **Tacoma**
- **\$100 Billion, \$65 Billion**
- **Food, noise, dust**
- **11,000 to 689,000 Children**



Who are these white guys?



What Is This?



Key Words

Dose / Response

Risk =

Hazard X Exposure

Individual Sensitivity



Paracelsus

**“All substances are poisons;
there is none which is not a poison.
The right dose differentiates a poison
from a remedy.”**

Paracelsus (1493-1541)

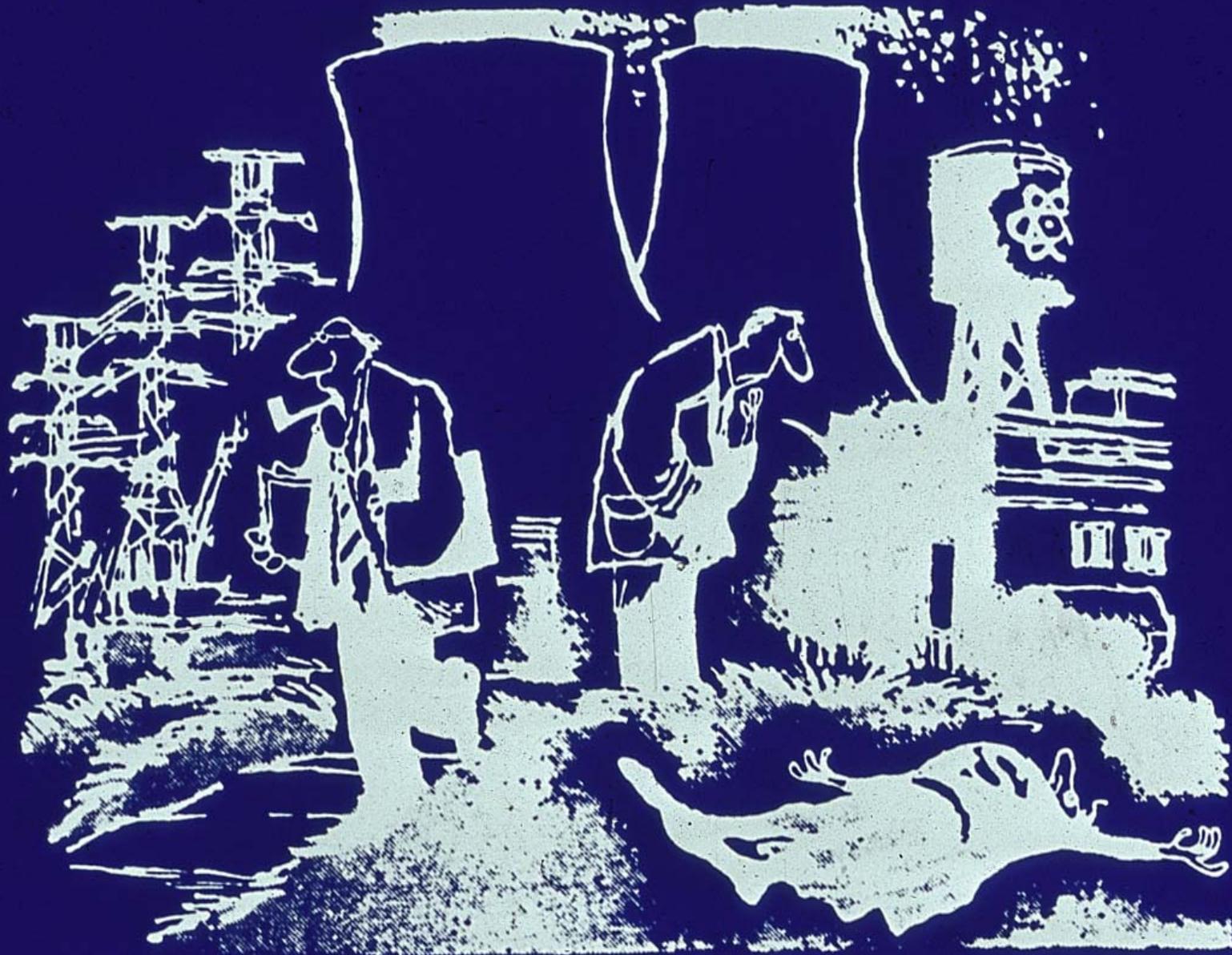


An Individual View

“The sensitivity of the individual differentiates a poison from a remedy. The fundamental principle of toxicology is the individual’s response to a dose.”

S. G. Gilbert (1997)





SO WHAT'S WRONG WITH RELEASING HARMLESS AMOUNTS OF KRYPTON GAS INTO THE ATMOSPHERE?..

Effects of Amount on Response



Effects of Size on Response



Life – Potential & Harm

**All life depends on
reproduction and
development.**

**What effects this process
and harms a child's
potential?**



Terms

- **Monster** – abnormal or strange animal or plant. From Latin monstrum omen, from monere to warn (abnormal infants reflect the future).
- **Teratology** – The study of malformations. From the Greek word for monster – teras.



Three Areas

- **Reproduction – issues associated with the egg and sperm**
- **Pregnancy – the critical environment of early development**
- **Development of the infant.**



Ancient Awareness

- **Many ancient cultures had fertility goddess**
- **Many ancient documentation of malformations**
- **Malformations rich aspect of mythology**
- **6500 BC – Turkey - figurine of conjoined twins**
- **4000-5000 BC – Australia drawings of twins**
- **2000 BC - Tablet of Nineveh – describes 62 malformations and predicts the future**



Historical Awareness

- **15th-16th centuries malformations caused by the devil, mother and child killed**
- **1830's - Etienne Geoffroy Saint-Hilaire experimented with chicken eggs**
- **1900's began acceptance of malformations related to genetics**
- **1940's - Josef Warkany – environmental factors affect rat development**



Historical Events

- **1941 – Human malformations linked to rubella virus**
- **1960's – Thalidomide (a sedative and anti-nausea drug) found to cause human malformations**
- **1950's – Methylmercury recognized as developmental toxicant**
- **1970's – Alcohol related to developmental effects – Fetal Alcohol Syndrome (FAS)**



Human Reproductive Facts

- **50% of pregnancies end in miscarriage or spontaneous abortion often before pregnancy is recognized**
- **15% of couples of reproductive age are infertile**



Reproductive Endpoints

- **Fertility**
- **Menstrual cycle**
- **Sperm count and viability**
- **Sexual behavior**



Reproductive Toxicants

- **Endocrine disruptors**
 - **DDT, Dioxin**
- **Heavy metals**
 - **Lead (decreased sperm)**
- **Organic Solvents**
 - **Toluene, benzene**
- **Drugs**
 - **Alcohol**



Pregnancy Effects the Women

- **Cardiovascular**
 - Increased - cardiac output heart rate, blood pressure, blood volume expands
- **Oxygen consumption increases by 15-20%**
- **Urine volume increases**
- **Gut absorption changes**
 - Increases in iron and calcium (toxic lead substitutes for calcium)
- **Liver metabolism decreases for some drugs or chemicals (caffeine)**



Developmental Endpoints

- **Teratology** (physical malformations)
- **Birth weight**
- **Growth**
- **Neurobehavioral**
 - **Decreased intelligence**
 - **Decreases learning and memory**



Metals

- **Lead**
- **Methylmercury**
- **Arsenic (in animals)**



Chemicals/Radiation

- **Chlorobiphenyls**
- **Solvents (Toluene)**
- **Endocrine disruptors**
 - **DDT, PCBs**
- **TCDD**

- **X-rays (therapeutic)**
- **Atomic fallout**



Infections/Medical Conditions

- **Rubella virus**
- **Herpes simplex virus**
- **Toxoplasmosis**
- **Syphilis**

- **Diabetes**



Plants

- **Skunk cabbage
(*Veratrum californicum*)
– sheep & cattle**
- **Parasites (frogs)**



Medical Drugs

- **Antibiotics (tetracyclines)**
- **Anticancer drugs**
- **Anticonvulsants (Valproic Acid)**
- **Lithium**
- **Retinoids (Vitamin A)**
- **Thalidomide**
- **Diethylstilbestrol (DES)**
- **Anticoagulants (Warfarin)**



Recreational Drugs

- **Alcohol (ethanol)**
- **Tobacco**
- **Cocaine**
- **Solvent abuse**



Case Studies

- **Thalidomide**
- **Ethanol (Alcohol)**
- **Methylmercury**
- **Lead**



Thalidomide

- **Introduced in 1956 as sedative (sleeping pill) and to reduce nausea and vomiting during pregnancy**
- **Withdrawn in 1961**
- **Discovered to be a human teratogen causing absence of limbs or limb malformations in newborns**
- **5000 to 7000 infants effected**
- **Resulted in new drug testing rules**

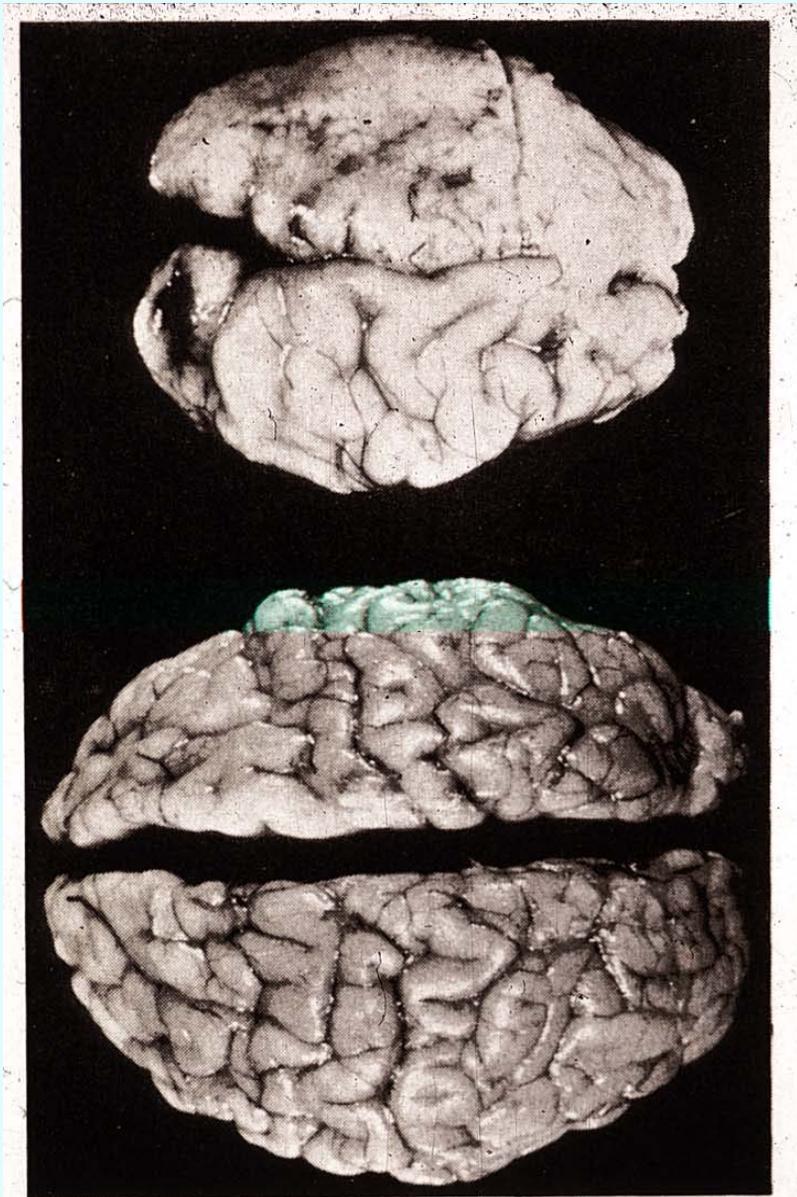


Ethanol (Alcohol)

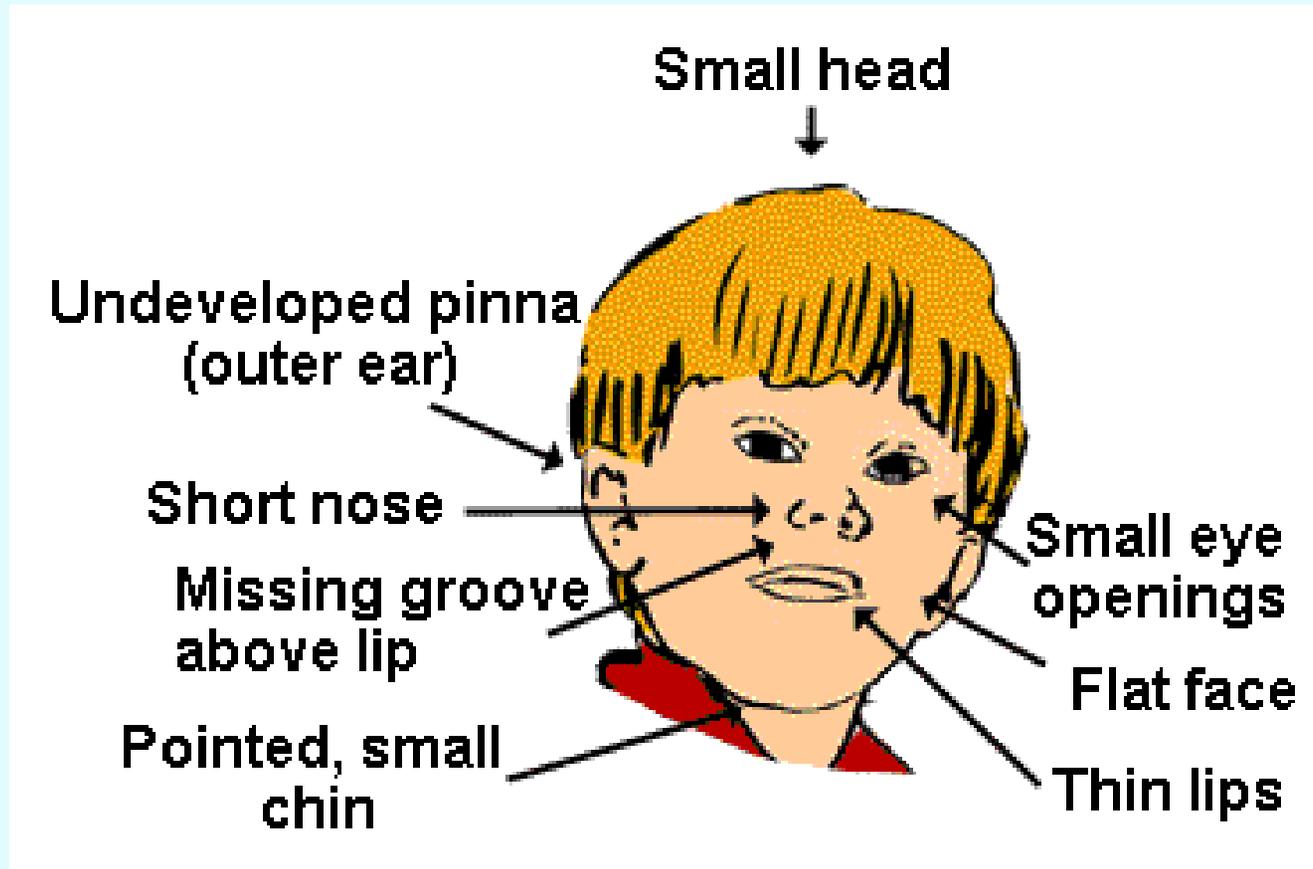
- **The common preventable cause of adverse fetal development**
- **Fetal Alcohol Syndrome (FAS) first described in 1970's**
- **Symptoms included facial deformities, growth retardation, severe nervous system effects and reduced intelligence**
- **4,000-12,000 infants per year in US**
- **Fetal Alcohol Effect (FAE) – milder form but still serious nervous system effects**



Effects of Prenatal Alcohol



Effects of Prenatal Alcohol



THE PREVENTABLE TRAGEDY

FETAL ALCOHOL SYNDROME

Text and photographs by GEORGE STEINMETZ



Mouse – Scanning EM

MOUSE FETAL ALCOHOL SYNDROME



NORMAL



FAS

Methylmercury (MeHg)

- **Mercury (quick silver) is converted to methylmercury by bacteria**
- **Methylmercury accumulates in fish, which are consumed by humans**
- **In 1950's the developmental effects of MeHg were first recognized in Minamata, Japan**
- **Across the world there a regulatory agencies set limits the amount of mercury in fish that is safe to consume**



Hg - Inorganic & Organic

Hg

Inorganic – Quick Silver

Hg — CH₃

Organic – Methyl Mercury



Discharge in Minamata Bay



Fetal Effects of MeHg



Life-Long Effects of MeHg



Iraq Infant - Effects of Mercury



Lead History

- **6500 BC. - Lead discovered in Turkey, first mine.**
- **100 BC. - Greek physicians give clinical description of lead poisoning.**
- **1904 - Child lead poisoning linked to lead-based paints.**
- **1922 - League of Nations bans white-lead interior paint; U.S. declines to adopt**
- **1923 - Leaded gasoline goes on sale in selected markets**
- **1971- U.S. Lead-Based Paint Poisoning Prevention Act passed**
- **1923 - Leaded gasoline goes on sale in selected markets**
- **1986 - Primary phase out of leaded gas in US completed**



Ancient Awareness

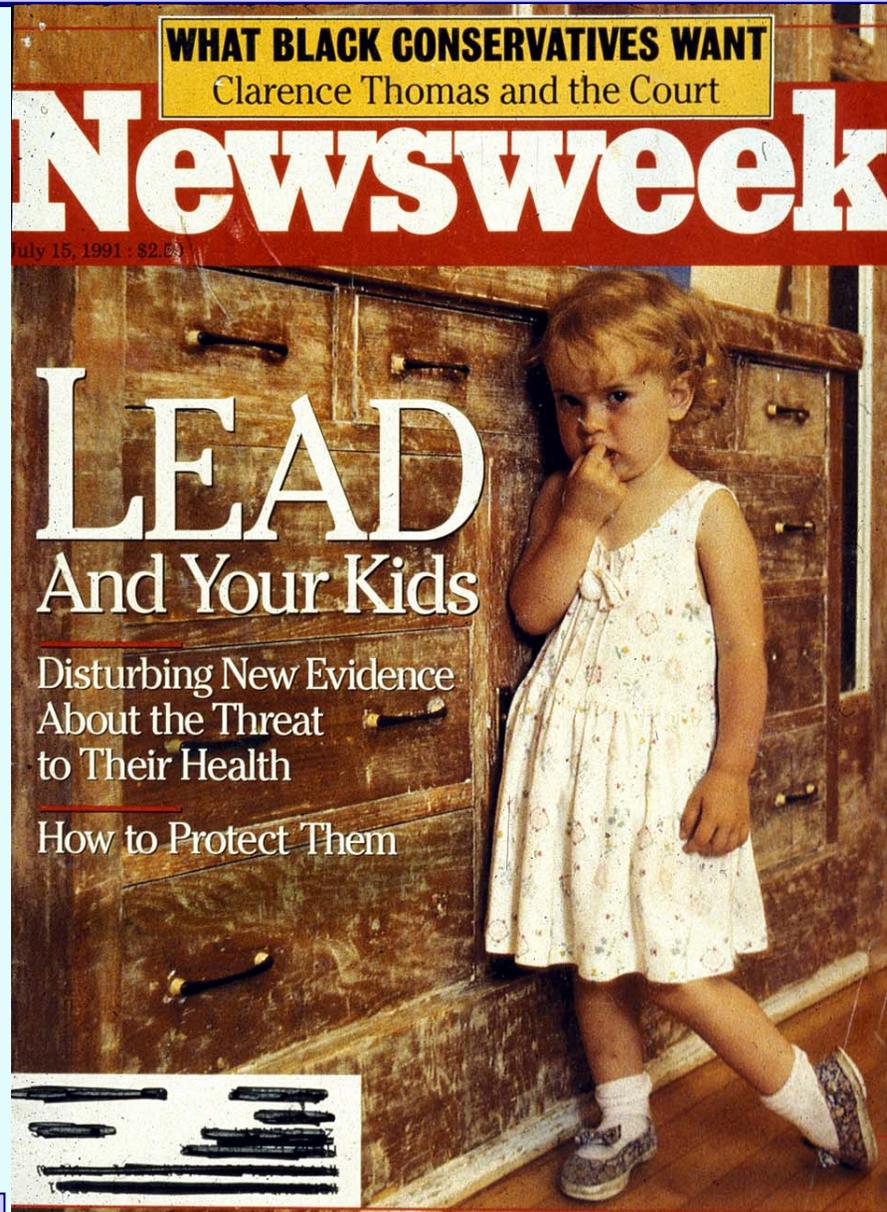
**"Lead makes the
mind give way."**

Greek

Dioscorides - 2nd BC



Lead In Homes

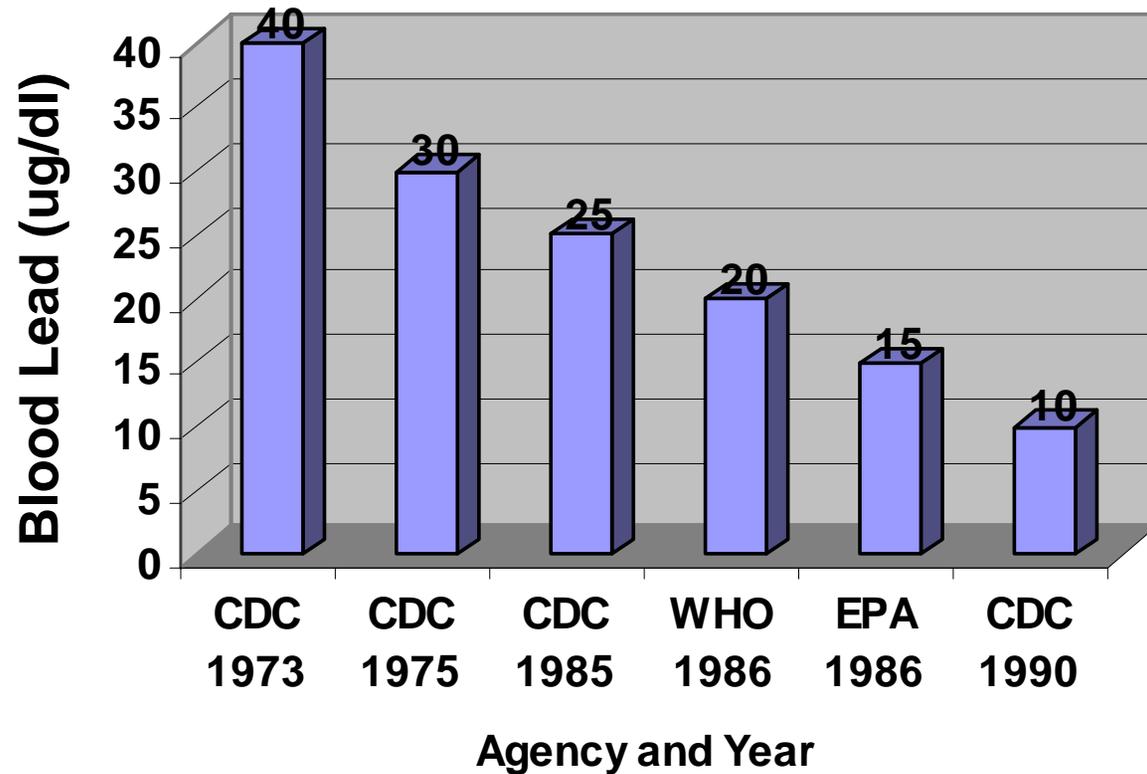


Lead in Families



Agency Blood Lead Levels

Acceptable Childhood Blood Lead Levels



Lead Health Effects

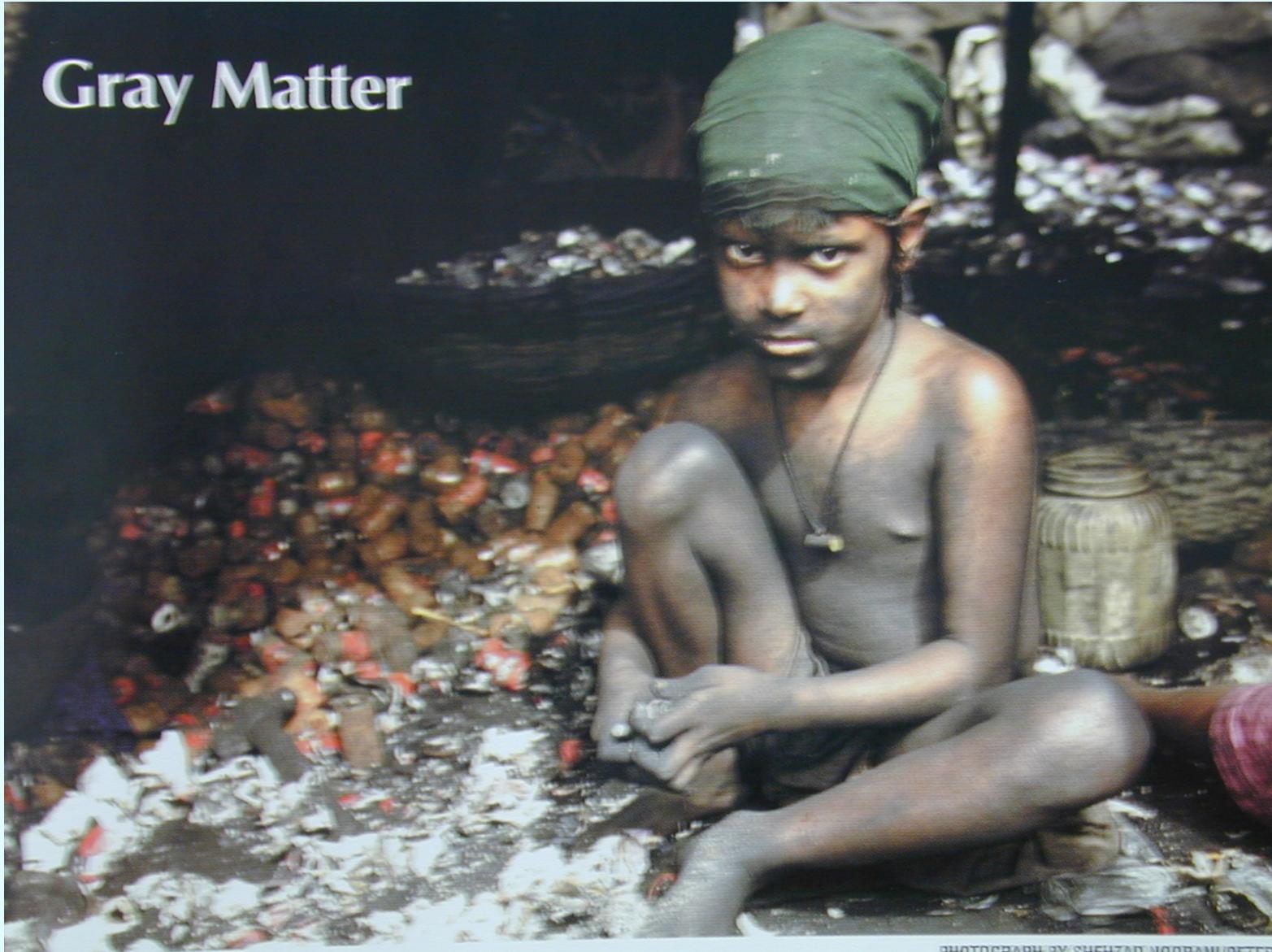
- **Children more vulnerable than adults**
 - Orally consumed lead absorbed in place of calcium
 - **CHILDREN** absorb 30-50% of oral lead
 - **ADULTS** absorb 5-10% of oral lead
 - Increased absorption during pregnancy

- **Childhood effects**
 - Decreased intelligence (lower grades)
 - Hyperactivity (higher school dropout rate)
 - Growth retardation
 - Effects at blood lead levels of 10 $\mu\text{g}/\text{dl}$



Recycling Lead

Gray Matter



PHOTOGRAPH BY SUECHIAN HONGDAM/DETER



Who is at Risk?

- **Women of childbearing age**
- **Pregnant women**
- **Men wishing to a parent**
- **Infants**
- **Children**



Exposure Issues

- **Home environment**
- **Drug use**
- **Workplace**
- **Global and local environment**

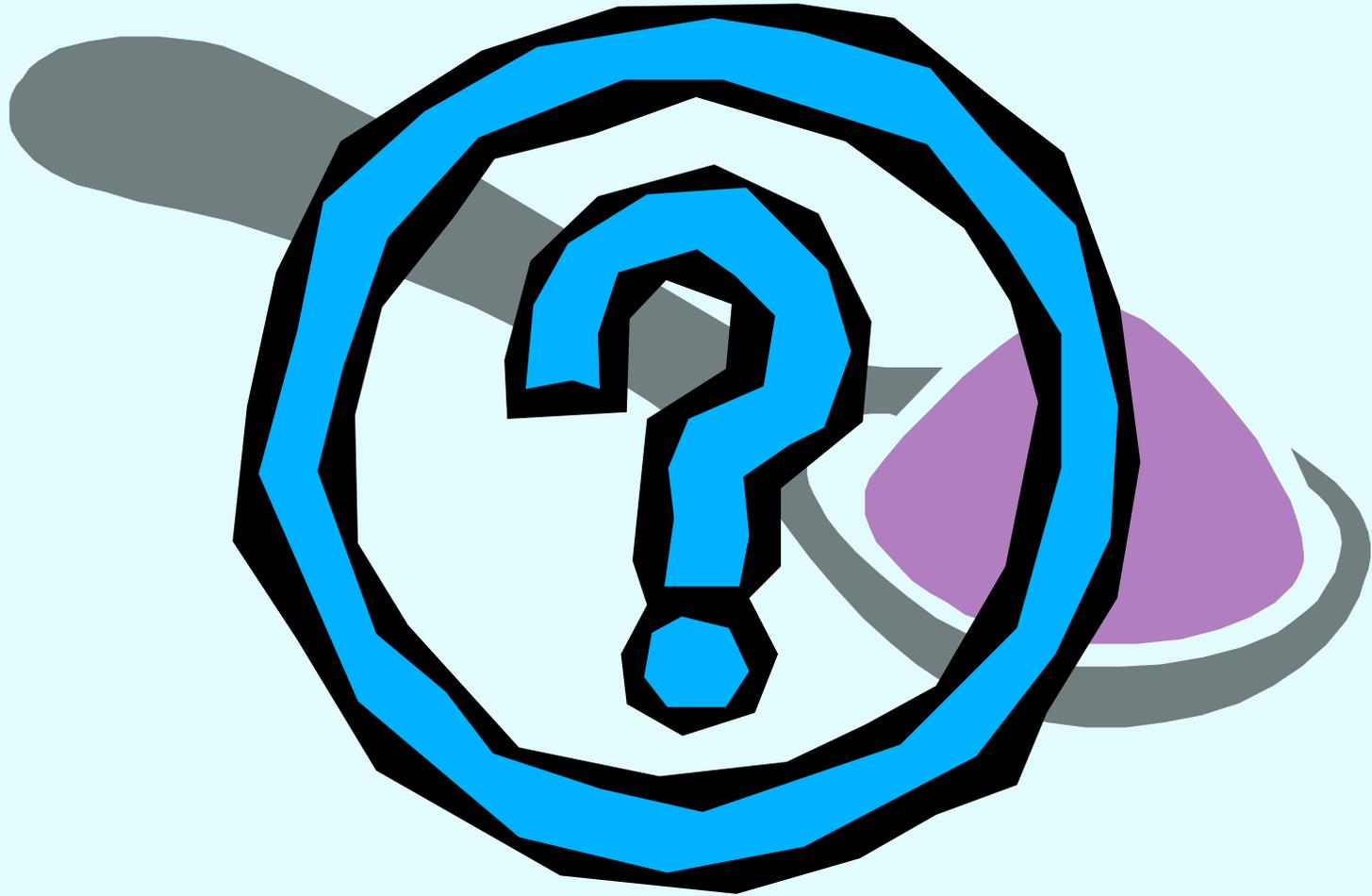


Regulatory Status

- **FDA – Reproductive and Developmental drug testing requirements**
- **EPA – Testing requirements**



A Small Dose of TM Developmental Toxicology



Additional Information

➤ Web Sites

- Teratology Society. Online. <http://teratology.org/>

➤ Other Chapters

- Mercury, Lead, Alcohol



Authorship Information

**This presentation is supplement to
“A Small Dose of Toxicology”**

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