Dioxin: Toxicity and Health Effects

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What is Dioxin?

- Chlorinated dibenzo-p-dioxins = a family of 75 chemicals
- Colorless, odorless solids
- Prototype is 2,3,7,8-TCDD (most toxic)
- Exist as mixtures (TEQ)
- Not intentionally manufactured
Sources

- Chlorine bleaching processes at pulp and paper mills
- Waste & drinking water treatment
- Chemical manufacturing contaminants
- Released into air in emissions
- Uncontrolled combustion of household wastes
Fate of CDDs

- Persistent
- Emissions: may be transported in air long distances
- Waste water: most attaches to soil - sediment
- Concentrate in food chain
- Overall environmental levels declining in US
Human Exposure

- 95% diet (meat, dairy, fish, breast milk)
- Proximity to hazardous waste site or incinerator
- Air, water, skin contact: less significant
- Occupational
- Half-life ~ 8.5 years
Dioxin Toxicity

- Potent animal toxicants
- Tremendous species variability
- Dioxins have a common toxic mechanism
- Alter basic steps for cell growth and development
- Results in broad impact in animals:
  - Reproductive/developmental
  - Immunologic
  - Skin
  - Cancer
Dioxin binds to AhR

AhR

XAP2

PM

HSP90 dimer

Nuclear Membrane

Transcription

ARNT

DNA

Gary Perdew www.cas.psu.edu/docs/CASDEPT/VET/ppl/perdew/pages/ah_rec.html
Human Toxicity

- Occupational studies (chemical workers)
- Accidents
  - Missouri, Italy, Asia
- Breast milk
  - Netherlands
- Vietnam veterans
Human Cancer

- Dioxin is a human carcinogen
- Exposure to TCDD increases the risk of cancer at multiple sites, including lung CA
- Overall increased risk in occupational/accident studies is 40-100%
- Possible association with STS
- Little if any association with NHL or skin CA
Human Non-cancer Effects

- **Good evidence**
  - Chloracne
    - Acute high level or chronic
    - Persists 10 years
  - Liver enzyme changes
    - No evidence for disease
    - Higher in drinkers
  - Reproductive hormone changes
    - Decreased testosterone
    - Decreased libido
Human Non-cancer Effects

- Possible effects
  - Blood lipids: ↑TG/cholesterol
  - Diabetes
  - Post-natal development
    - Neurobehavioral
    - Thyroid
    - Liver enzymes
    - Platelets
Human Non-cancer Effects

- Good evidence in animals, but human data inconclusive
  - Circulatory
  - Immunologic
    - No change in children of Seveso at 2 years
    - Limited data on depressed T-cell function
  - Semen changes
  - Endometriosis
Human Non-cancer Effects

- **Emerging Issues: further study needed**
  - Miscarriage rate
  - Birth defects
    - Majority studied are paternal exposures
    - Misclassification may have occurred
  - **Dental effects**
  - Sex ratio
  - **Growth measures**
    - Decreased length (transient) & birth weight
    - Increased preterm birth & neonatal death rate
Human Non-cancer Effects

- Lack of evidence for:
  - Long-term thyroid gland effect
  - Renal effect
  - Pulmonary effect
  - Adult neurologic effect
General Population Body Burden

- Estimated to be 25 ppt (pg TEQ/g lipid)
- Approaches the levels at which adverse events are expected
- No clear indication of disease
- Scientific limitations
- Increased risk of cancer may be 1: 1,000 increased chance
Children may be at greater risk for illness related to environmental contaminants

- Increased outdoor play
- Increased hand-to-mouth activities
- Shorter stature - dust, soil, vapors
- Higher intake rate, lower body weight = greater dose
- Critical, rapid growth stages
- Latency
Midland

- **Michigan vital statistics & MRCIF**
  - No persistently elevated numbers of specific cancer types
  - Higher than expected numbers of all cancers combined for zip code 48640
Midland

- MBDR
  - No increased anencephaly, spina bifida, cleft lip in Midland County
  - Limitations
Special Populations

- Fetuses, infants and children may be more susceptible based on rapid growth & development
- Unknown whether children in the general population are experiencing health effects from dioxin
- Immunocompromised
Prevention

- Avoid contact with soils near contaminated or hazardous waste sites
- Discourage children from eating dirt/putting toys in their mouth, hand hygiene
- Diet
  - Fish advisory
  - Avoid food sources from contaminated areas
  - Wash & peel fruits & vegetables from contaminated areas
- Smoking/alcohol
- Recreation
- Do not stop breast feeding