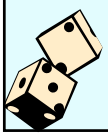
Getting Out of the Risk Assessment Box: Precautionary Approaches to Protect Health

Critical Analysis of Risk Assessment & Alternative Approaches



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Outline

Risk Assessment – Arbitrary and Capricious

- Principles of Risk Assessment
- Risk Assessment - examples
- Weaknesses of Risk Assessment
- Beyond Risk Assessment to Precautionary Assessment

Key Words of Toxicology

Dose / Response

Hazard X Exposure = Risk

Individual Susceptibility

Early Risk Assessment

"What is food to one man may be fierce poison to others."

Lucretius (c. 99 B.C.–c. 55 B.C.)

Perspective

"If someone had evaluated the risk of fire right after it was invented, they may well have decided to eat their food raw."

Julian Morris of the Institute of Economic Affairs in London

Modern Risk Assessment

- Developed in 1960-1970s
- Concern over increased cancer rates
- Expanded to non-cancer effects

Quantitative Risk Assessment

Process of estimating association between an exposure to a chemical or physical agent and the incidence of some adverse outcome.

National Research Council, Risk Assessment in the Federal Government: Managing the Process. National Academy Press, Washington, DC, 1983

Steps in Risk Assessment

- Hazard Identification
- Exposure Assessment
- Dose-Response Assessment
- Risk Characterization

What Hazard?

Obvious

Death, Cancer, Acid burn, Birth defect, asthma …..

Subtle

Decreases in learning and memory (lead)

Loss of potential

Sensitivity of the individual (child)

Hazard Identification

Review human and animal data to determine if a chemical or agent has biological effects.

Toxicity Endpoints

- Carcinogenicity
- Mutations
- Altered immune function
- Teratogenicity
- Altered reproductive function
- Neuro-behavioral toxicity
- Organ-specific effects
- Ecological effects (wildlife, environmental persistence)

Exposure Assessment

- Route of exposure (skin, oral, inhalation)
- Amount of exposure (dose)
- Duration of exposure
- To whom (animals, humans, environment)
- Children, other sensitive individuals

Exposure Issues

- Home environment
- Workplace (occupational)
- School
- Food
- Consumer products
- Global and local environment

Dose-Response Assessment

How much exposure to a chemical or agent will cause what effect?

Dose – Response

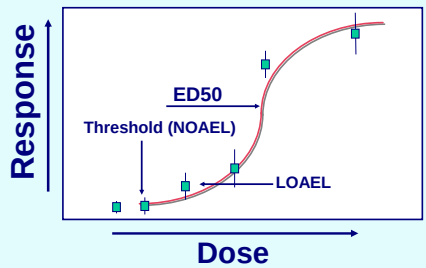
Some Jargon

LOAEL – Lowest Observed Adverse Effect Level (mg/kg)

NOAEL – No Observed Adverse Effect Level (mg/kg)

RfD – Reference Dose (mg/kg-day)

Greater Dose – Greater Response



Risk Characterization

Risk = Hazard X Exposure

- Hazard (including sensitive populations)
  - Low dose extrapolation
- Exposure
  - Route of exposure, amount, duration
    - dermal, oral, inhalation, injection
  - To Whom? Sensitive Individuals?

Doubt / Uncertainty

"Doubt is our product since it is the best means of competing with the 'body of fact' that exists in the mind of the general public."

1969 an executive at Brown & Williamson owned by R. J. Reynolds Tobacco Company

(*Doubt Is Their Product* by David Michaels in Scientific American, June 15, 2005)

Uncertainty

- Measurements error in experiments
- Extrapolation from animal studies to human
- Sample sizes for animal and human studies
- Selection of endpoint
- Intra and inter subject variability

Human Variability

Human Subject Variability

- Lifestyle – risk of exposure to ….
- Occupation – risk of exposure to ….
- Breathing & digestion – uptake of chemicals
- Metabolism & kidney function – elimination
- Age, gender & disease – susceptibility to toxicity
- Socio/economic facts

Examples of Variability

- Children spend more time on floor – more hand to mouth behavior than adults
- Rate of breathing higher in children than adults
- Occupation – exposure to other chemicals
- Lung function and susceptibility are altered by smoking or asthma
- Disease effects liver function

The overall dose-response behavior is subject to both intra-individual and inter-individual variability.

Use of Uncertainty Factors

Divide Dose by Power of 10

- Human variability
- Interspecies extrapolation
- Children
- Subchronic to chronic extrapolation
- Absence of a NOAEL
- Database uncertainty

Use of Uncertainty Factors

Animal Dose Response Data

NOAEL (No Observed Adverse Effect Level) or LOAEL

↓

Divide by 10

(Account for inadequate animal data)

↓

Divide by 10

(Animal to Human Extrapolation)

↓

Divide by 10

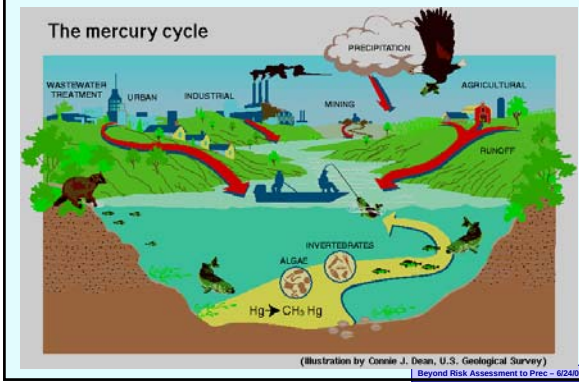
(Human Variability or Individual Sensitivity)

↓

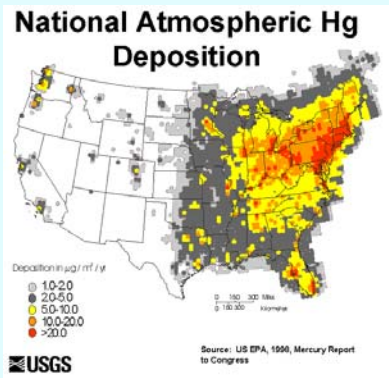
Reference Dose (RfD) Or Acceptable Daily Intake (ADI)

Mercury & Toxicology

The Mercury Cycle



Atmospheric Hg



Neurobehavioral Effects

- Blindness - Deafness
- Cerebral Palsy - Seizures
- Abnormal reflexes & muscle tone
- Retarded motor development
- Visual and Auditory Deficits
- Delayed motor development
- Human and animal data

Effects On The Brain

- Decrease in Brain Size
- Cell loss
- Disorganization of cells
- Cell migration failures
- Behavioral effects – learning and memory

Fetal Effects of MeHg

Animal - Risk Assessment

- MONKEY - 25 µg/kg - LOAEL
- RAT - 10 µg/kg - LOAEL
- RAT - 50 µg/kg - replicated

Animal - Risk Assessment

- 2.5 µg/kg - NOAEL (animals)
- 0.25 µg/kg - Human
- 0.025 µg/kg - Sensitive populations

(the rule of dividing by 10)

Human - Risk Assessment

• 10-20 ppm hair - LOAEL •
• 40-80 ppb blood - LOAEL •
• 0.645 µg/kg •
• 0.06 µg/kg - RfD •

Gilbert, S.G., and Grant-Webster, K.S. Neurobehavioral effects of developmental methylmercury exposure. Env. Health Persep. 103(Suppl 6), 135-142, 1995.

MeHg Consumption Limits

US EPA – 0.1 ug/kg-day

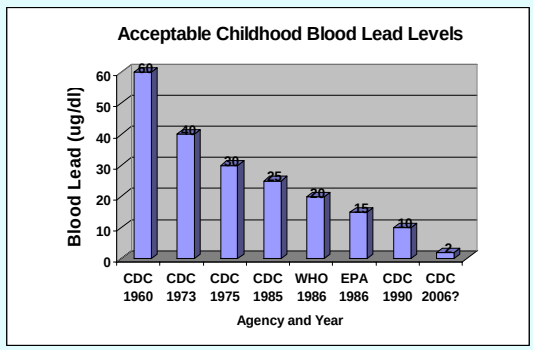
US FDA – 1 ppm (mg/kg) in tuna

Ancient Awareness

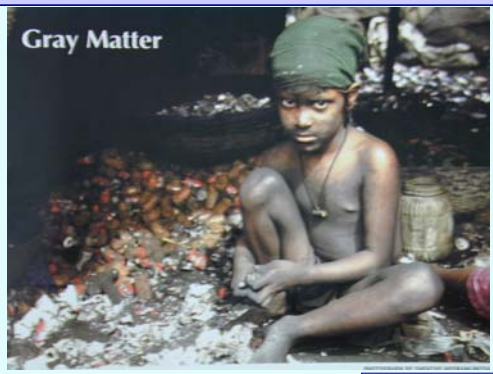
"Lead makes the mind give way."

Greek
Dioscerides - 2nd BC

Agency Blood Lead Levels



Recycling Lead



Limitations of Risk Assessment

- Lack of adequate data
- Most sensitive endpoint
- Low dose extrapolation
- Exposure information
- Multiple chemical exposures
- Complex – expert driven – undemocratic
- Individual sensitivity
- Narrow perspective – Ethical??

Precautionary Assessment

An approach to evaluating the scientific, safety, community, ethical, and social issues related to a compound or procedure.

- Community / Social Issues
- Exposure Issues
- Hazard / Toxicity

Precautionary Assessment

Goals of PA

- Place the knowledge available within the context of the community.
- Incorporate the communities knowledge, values, and ethics into a more comprehensive evaluation of a hazardous condition.
- **Shift the burden of response.**

PA – A Work in Progress

- Your comments and feedback are welcome.

Following work sheets:

- PA-defined: defined the elements, questions, and scoring.
- PA-worksheet: a sample worksheet that can be copied and edited with a compound of your choice.
- PA-Lead: A precautionary assessment of lead.
- PA-Water: A PA of water.

Precautionary Assessment

- Community / Social Issues
  - G = Goal
  - N = Need
  - F = Future Generations
  - D = Democratic, community based process
  - A = Alternatives

Precautionary Assessment

- Exposure Issues
  - E = Exposure
  - M = Multiple exposures
  - Ch = Children exposed
  - CP = Consumer products
  - O = Occupational exposure
  - F = Food exposure

Precautionary Assessment

- Hazard / Toxicity
  - H = Hazard
  - IS = Individual Sensitivity
  - EC = Ecological hazard
  - V = Volume
  - P = Persistent
  - B = Bioaccumulate
  - UC = Uncertainty

Precautionary Assessment

Lead

- Community / Social Issues - 12/15
- Exposure Issues – 16/20
- Hazard / Toxicity – 27/30

Rights and Policy

- We have a right to an environment in which we can reach and maintain our potential
- A matter of POLICY not Risk Assessment

The Potential of Children

Additional Information

- National Research Council, Risk Assessment in the Federal Government: Managing the Process. National Academy Press, Washington, DC, 1983
- World Health Organization - The International Programme on Chemical Safety (IPCS) – Risk Assessment –http://www.who.int/pcs/ra_main.html
- U.S. Environmental Protection Agencies - National Center for Environmental Assessment (NCEA) – http://cfpub.epa.gov/ncea/
- A Small Dose of Toxicology – Risk Assessment - http://www.asmalldoseof.org/toxicology/risk_assessment.php

Risk Assessment

Fundamental Uncertainty

- Not knowing the right questions to ask
- Most sensitive end point
- "we don't know what we don't know"

Sir Austin Bradford Hill

"All scientific work is incomplete - whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us a freedom to ignore the knowledge we already have or postpone the action that it appears to demand at a given time. "

Sir Austin Bradford Hill (1965)

Determining Causation

1. Strength of association
2. Consistency of findings
3. Biological gradient
4. Temporal sequence
5. Biologic or theoretical plausibility
6. Coherence with established knowledge
7. Specificity of association

Sir Austin Bradford Hill (1965)

Characteristics of Risk

Characteristic	Level	Examples
Knowledge	Little known	Food additives
	Much known	Alcoholic drinks
Newness	Old	Guns
	New	Space travel
Voluntariness	Not voluntary	Crime
	Voluntary	Rock climbing
Control	Not controllable	Natural disasters
	Controllable	Smoking
Dreadedness	Little dread	Vaccination
	Great dread	Nerve gas
Catastrophic potential	Not likely	Sunbathing
	Likely	War
Equity	Distributed	Skiing
	Undistributed	Hazardous dump

Adapted from Kraus and Slovic (1988), Risk Anal., 8: 435.

Risk Perceptions