ENVSC 296: Lesson No. 3

Tools for Env. Health

January 10, 2005

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Lesson Overview

- Toxicology
  - Basic Principles
  - Chemicals and Cancer
- Risk
  - Assessment
  - Management
  - Communications

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Toxicology

Basic Concepts

Types of information used to determine chemical risks to humans

- **Human Epidemiology data**
- **Laboratory Animal Data**
- **Chemical Structure Analysis**

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Fundamental Rules

1. "The Dose Makes the Poison"

"All substances are poisons. There are none that are not. The dose separates the remedy from the poison."

Paracelsus
(Theophrastus Bombastus von Hohenheim, 1493-1541)

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Fundamental Rules

2. Exposure must occur for the chemical to present a risk

3. The magnitude of risks is proportional to both the *potency* of the chemical and the *extent* of exposure

Risk = Hazard x Exposure

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Routes of Exposure

1. **Direct Exposure**
   (through Use and/or Accident)
   a) **Ingestion**
      (children; intentional)
   b) **Skin contact**
      (e.g., acids, solvents, pesticides)
   c) **Inhalation**
      (e.g., paints, pesticides)

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Exposure Routes Continued

2. **Indirect Exposure**
   a) **Contamination of drinking water**
   b) **Contamination of soil / house dust**
   c) **Contamination of indoor air**

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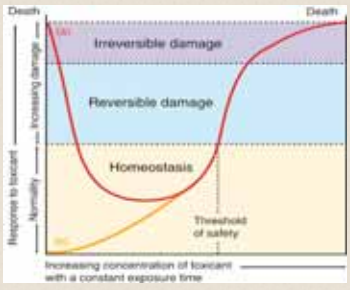
Dose-Response Relationship



Range of possible dose-responses in an individual

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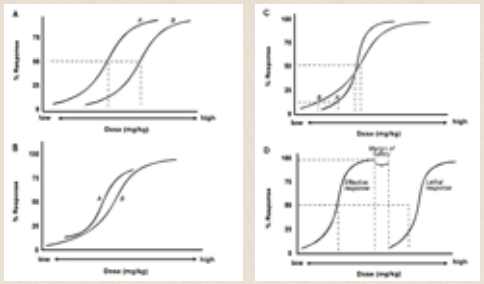
Potency & Dose-Response



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LD_{50} of Representative Substances

TOXIC AGENT	*LD 50*	*TOXICITY RATING*
Ethanol	10,000	Slightly Toxic
Sodium chloride	4,000	Moderately Toxic
Phenobarbital	150	Very Toxic
DDT	100	Very Toxic
Parathion	7	Extremely Toxic
Nicotine	1	Super Toxic
Curare	0.05	Super Toxic
Dioxin (TCDD)	0.001	Super Toxic
Botulinum Toxin	.00001	Super Toxic

Chemical Interactions

- **Additive:** 2 + 3 = 5
- **Synergistic:** 2 + 3 = 20
- **Potentiation:** 0 + 2 = 10
- **Antagonism:** 4 + 6 = 8
  4 + (-4) = 0
  4 + 0 = 1

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NOAEL
(No Observed Adverse Effect Level)

- Determined from repeated dose experiments
- Identify highest dose used (of 4-6 groups) that produces no evidence of adverse effect
- Used by regulatory agencies to establish "acceptable" doses (e.g., FDA's "ADI")
- Safety Factors (or Uncertainty Factors) are used to adjust animal NOAEL to Human dose

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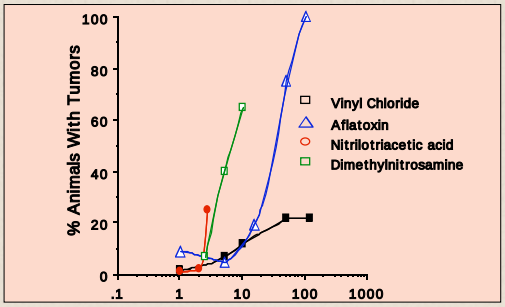
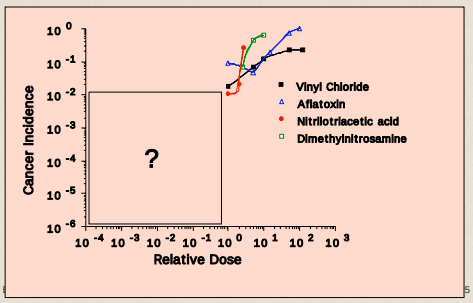
Setting the Safe Dose



Setting the Safe Dose



What are "Mutations"?

- Mutations refer to irreversible changes in the DNA (our "genes") of a cell
- Mutations arise when reactive molecules in the cell bind to and damage DNA
- Each cell in the body experiences thousands of potentially damaging changes each day

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What are "Mutations"? Continued

- Nearly all of this damage is "repaired"
- If damage is not repaired, (or is repaired incorrectly), a permanent change in DNA occurs

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What are "Genes"?

- Genes are a stretch of DNA (a "sequence") that "codes" for a specific protein
- There are about 100,000 different genes in humans; each cell contains a copy of all
- Each gene has a specific function, but only a small number are used ("expressed") in any given cell
- Each cell has two copies ("alleles" of each gene - one from each parent)

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How do mutations occur?

- Most mutations occur "naturally" during the burning of sugar and oxygen to produce energy
- Certain chemicals in the environment can also interact with DNA and cause mutations
- Such chemicals are found in food, polluted air, drinking water, cigarette smoke, the workplace
- However, the body has certain defenses that help to detoxify these potential cancer causing chemicals

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What mutations cause disease?

- Only a small fraction of mutations result in diseases…such as cancer
- Certain genes, called "oncogenes" function normally to control cell growth, and are tightly regulated in the cell (usually "off")
- Certain mutations can switch an oncogene from "off" to "on", causing cells to grow abnormally
- Thus, mutations in one or more oncogenes is necessary, but not sufficient, to cause cancer

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What mutations cause cancer?

Continued

- Other genes, called "tumor suppressor genes" function normally to stop cells from dividing
- both copies of a tumor suppresor gene must be lost to loose this function
- Cancers arise when one or more oncogenes is "activated", and both copies of one or more tumor suppresor genes is inactivated
- Occasionally, these changes can be inherited, rather than acquired through mutation

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What Can You Do To Reduce Your Cancer Risk?

- *Don't smoke*
- Eat diets high in fruits and vegetables
- *Don't smoke*
- Drink only in moderation
- *Don't smoke*
- Learn about workplace hazards and use proper precautions/protective equipment
- Be a 'good citizen' of the environment

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Summary

Toxicology is the study of the adverse effects of chemical agents

1. Dose-Response Relationship
2. Risk = Potency X Exposure
3. Acute vs. Chronic Responses
4. Cancers and other diseases

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Risk

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Understanding Risks

- Hazard identification
- Dose-response assessment
- Exposure assessment
- Risk Characterization
- Risk Management

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Translation

- Is there a potential problem?
- What is the problem?
- Who has the problem?
- How bad is the problem?
- What should we do about it?
- Who and what do we tell?

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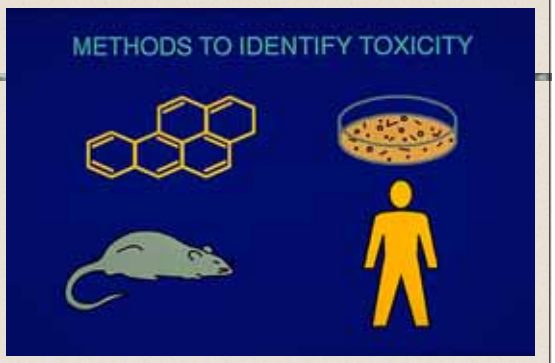

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Translation

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Comparing Risks

- Probability
- Expected Value
- Exposure
- Outrage
- Experts

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Comparative Risks

Event	Annual Risk
Car injury	1:100
Killed hang gliding	1:1,000
Killed mountain climbing	1:1,585
Cancer: 1 diet cola/day	1:10,000
Cancer: 4 tbsp. peanut butter/day	1:100,000

Event	Lifetime Risk
Hit by Lightning	1:631,000
Cancer: drinking chlorinated water	1:1,000,000
Win state lottery grand prize	1:10,000,000
Win Readers Digest sweepstake	1:250,000,000

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Comparing Risks

- Activities that increase annual risk by 1:1,000,000
  - Smoke 1.4 cigarettes
  - Drink 0.5 liters of wine
  - Live 2 days in New York or Boston
  - Live 2 months with a cigarette smoker
  - Live 150 years within 5 miles of a nuclear power plant

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Comparing Risks

- Voluntary *vs.* Involuntary Risks
- Immediate *vs.* Delayed Effects
- Common *vs.* Rare (Dread) Events
- Affects Everyone *vs.* Special Groups
- Reversible *vs.* Irreversible Effects

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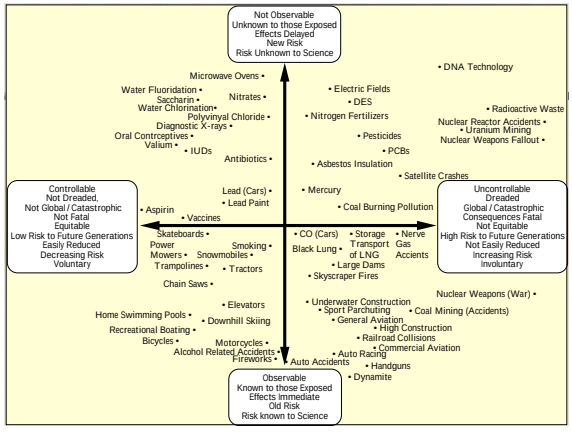

Changing Risks

- Understand the risks
- Understand who is at risk
- Characterize the risk
- Consider the alternatives
- Consider "protective" measures
- ACT!!!

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Cost-Benefit Analysis

Definition: A systematic attempt to compare the costs with the anticipated benefits of a technology, product, substance or process.

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Cost-Benefit Analysis

- List adverse consequences
  - assign probabilities
  - estimate cost of consequences
- List Benefits
  - assign probabilities
  - estimate gains/value of benefits
- Probability X Cost or Gain = Sum
- Compare cost *versus* benefits

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Cost-Benefit Analysis

- **Advantages**
  - Flexible
  - Easily scrutinized
- **Disadvantages**
  - Unrealistic assumptions
  - All consequences can not be anticipated
  - Probabilities are often unknown
  - Assigning price tags is difficult

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Cost-Benefit Analysis

Examples of Regulations Evaluated by Cost per Life Saved

Regulation	Status & Year	Annual Risk Estimate	Lives Saved Annually	Cost per Life Saved
Asbestos	Final 1972	4 in 10^4	296	$7,400
Benzene	Final 1984	9 in 10^4	4	$17,100
Asbestos	Final 1978	2 in 10^3	12	$92,500
Formaldehyde	Prop. 1983	7 in 10^7	<1	$72,000,000

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What is Risk Communication?

- **Part of the overall risk management process with…..**
  - Hazard identification
  - (recent: Risk Communication)
  - Determination of dose-response
  - Risk characterization
  - (traditional: Risk Communication)
  - Risk reduction

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Definitions

- Hazard
  - Something that can hurt you
- Risk
  - The likelihood (chance) that it will hurt you
- Risk Communication
  - Assisted dialogue among stakeholders

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Definitions (cont'd)

- Stakeholder
  - Anyone with interest in issue
- Worldview
  - How you see the world around you (why?)

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Risk Perception

- Perception = Reality (key concept)
- Goal (RC)= better understanding, thus acceptance, of risk
- Why do we perceive risks the way we do?

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Factors influencing risk perception

- Voluntary
- Control
- Fair
- Trustworthy Source
- Not Catastrophic
- Not dreaded
- Familiar
- Ethical
- Natural
- Explainable
- Detectable

- Involuntary
- Out of your control
- Unfair
- Untrustworthy source
- Catastrophic
- Dreaded
- Unfamiliar
- Unethical
- Artificial ("man" made)
- Hard to understand
- Undetectable

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What is Risk Communication? Seven Rules-→

- Reaching consensus about (chemical) risks
  - Involve the audience
  - Plan carefully and evaluate performance
  - Listen to the audience
  - Be honest, frank and open
  - Coordinate with credible sources
  - Speak clearly and with compassion
  - (Meet the needs of the media)

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When is Effective Risk Communication Needed?

- Low Trust/High Concern Environments (LT/HC)
  - Community concerns over environmental contamination
  - Worker concerns over chemical exposures
  - Patients learning that they are terminally ill
- Also: high trust/low concern scenario

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Characteristics of Low Trust / High Concern Environment

- Perception = Reality
- Emotions dominate ability to think rationally
  - Every communication principle is reversed in this environment
  - Everything that's natural and instinctive is wrong
- Goal is to create trust and establish credibility
- Communication = Skill

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Current Federal Issues

- Risk and Regulation
- Cost-Benefit Analysis
- Precautionary Principle

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For Additional Study

- Web sites:
  - National Toxicology Program - *http://ntp-server.niehs.nih.gov/*
  - Society for Toxicology - *http://ntp-server.niehs.nih.gov/*
- Readings:
  - Murphy SD. "Some Concepts in Toxicology", *Environmental Health Perspectives*, October 1979:261-266.
  - Ott WR, Roberts JW. "Everyday Exposure to Toxic Pollutants", *Scientific American*, 278(2):86-91.
  - Wong O, Bailey WJ. "Cancer Incidence and Community Exposure to Air Emissions from Petroleum and Chemical Plants in Contra Costa County,California: A Critical Epidemiological Assessment." *Journal of Env. Health*, December 1993, 56(5):11-17.

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Next Lesson

Environmental Health Tools II:

Statistics, Epidemiology & GIS

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