Lesson 6. Toxicology & Risk

Part I. Toxicology: Basic Concepts & Applications

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Lesson Overview

- What is Toxicology?
- Basic Principles that determine toxic responses to chemicals in our environment
- Chemicals and Cancer

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Lesson Objectives

- Explain how scientific information is collected and used to identify and eliminate human health hazards from chemicals in the environment
- Discuss the major causes of cancer, and how chemicals contribute to cancer risk

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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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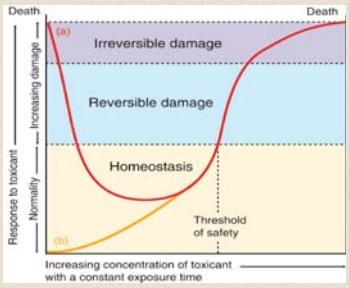
Dose-Response Relationship



The "individual", or continuous, dose-response curve

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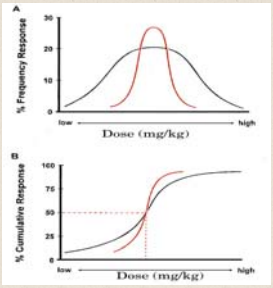
Dose-Response Relationship



The Frequency Distribution Curve

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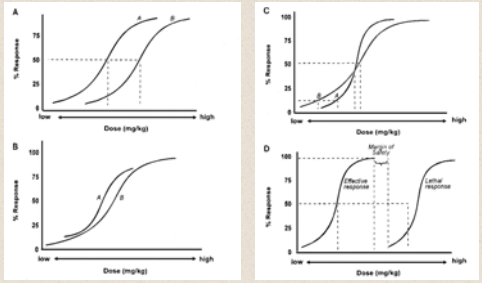
Potency & Dose-Response



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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

- Functional; Chemical; Dispositional; Receptor

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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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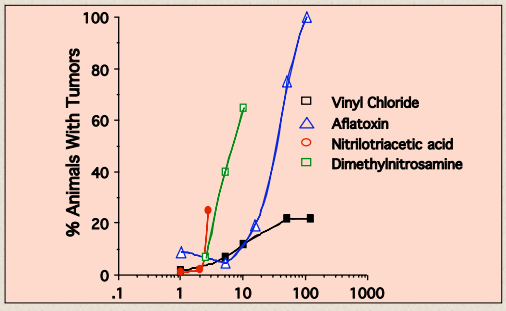
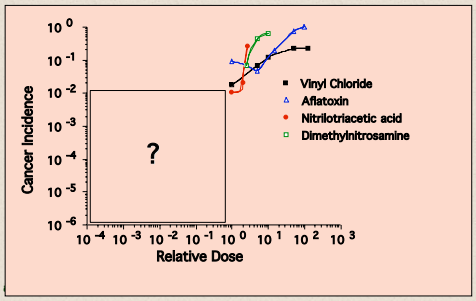
Setting the Safe Dose



Setting the Safe Dose



Cancer

- Cancer refers to a chronic disease process characterized by the uncontrolled growth of cells (tumors), that may spread (metastisize) throughout the body, ultimately causing death
- Cancer arises when the DNA in a cell is altered -- a process called "mutation"

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Who gets Cancer?

- 1 out of 3 people living today will get cancer in their lifetime; 1 out of 4 will die from it
- In the US, nearly 500,000 people will die from cancer this year; 2nd leading cause of death
- Cancer is largely a disease of "old age"
- Cancer is a disease process affecting different organs; not a single disease

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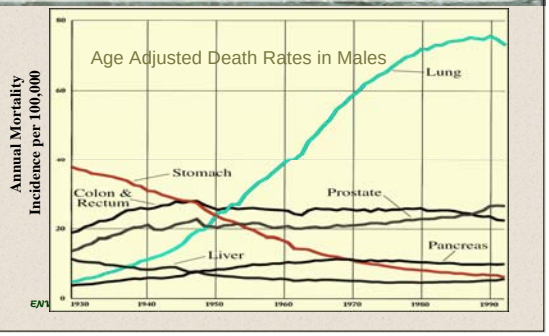
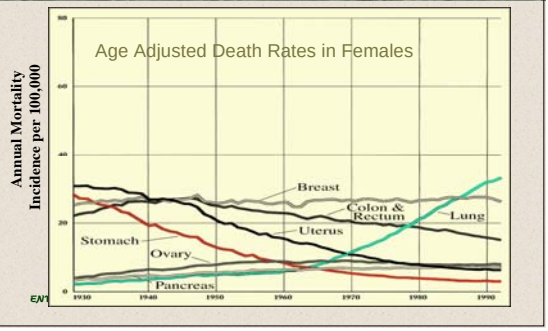
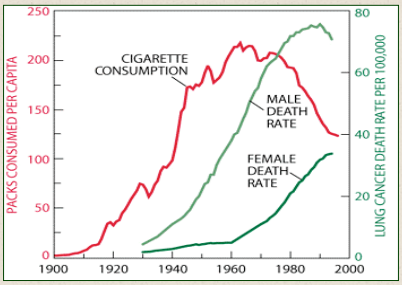
Cancer Deaths



Cancer Deaths



Smoking & Cancer



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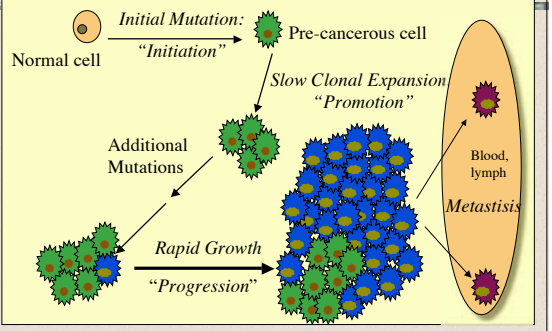
The Multi-step Process of Cancer



Cancer Risk Factors

Proportion of cancer death attributed to various factors

FACTORS	BEST ESTIMATE (%)	RANGE (%)
Tobacco	30	25 - 40
Alcohol	3	2 - 4
Diet	35	10 - 70
Food additives	< 1	-5 - 2
Reproductive/sexual behavior	7	1 - 13
Occupation	4	2 - 8
Pollution	2	<1 - 5
Industrial Products	<1	<1 - 2
Medicines/medical procedures	1	0.5 - 3
Geophysical factors (e.g., radon)	3	2 - 4
Infection	10?	1 - ?

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

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Questions

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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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Lesson 6. Toxicology & Risk

Part II. Risk: Assessment and Management

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Uncertainties in Life

"One of the brightest gems in the New England weather is the dazzling uncertainty of it."

. . . Mark Twain

Objectives

- **Understand perceptions of risk vary**
- **What is a risk assessment and what are the components of a risk assessment?**
- **Risk assessment approaches**

Why do Risk Assessments?

- We know that

  Risk = Hazard x Exposure

- We use a risk assessment to quantitatively and qualitatively define an exposure that may lead to an adverse effect and use this information to minimize accident or illness

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Understanding Risks

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

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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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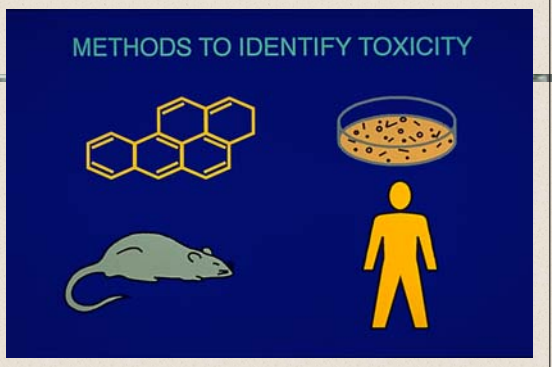

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Comparing Risks

- Probability
- Expected Value
- Exposure
- Outrage
- Experts
- Avoidance

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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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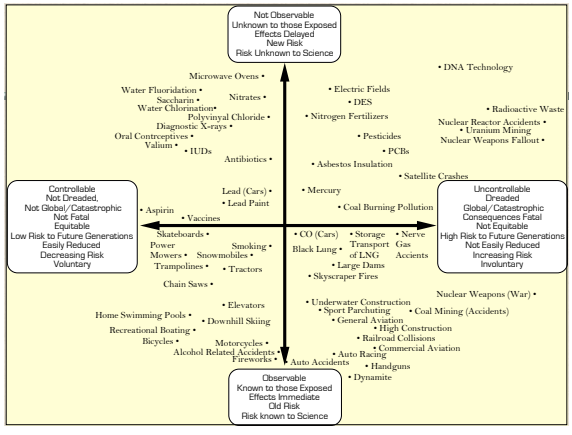


Changing Risks

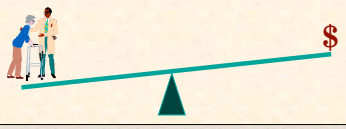
- Understand the risks
- Understand who is at risk
- Characterize the risk
- Consider the alternatives
- Consider "protective" measures
- ACT!!!

Risk Assessment Approaches

- Cost-benefit analysis
- Revealed preference
- Expressed preference
- Natural standards

Cost-Benefit Analysis

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



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

"Veg-E-Wax"

Benefits	Anticipated Value
Storage loss prevented	1,000,000
Nutritive value preserved	800,000
Total	$1,800,000

Costs	Anticipated Value
Application costs	100,000
Cancer in workers	100,000
Cancer in consumers	100,000
Unappealing appearance	1,600,000
Total	$1,900,000

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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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Revealed Preferences

Definition: The acceptable risk for a new technology is the level of safety associated with ongoing activities having similar benefits to society.

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Revealed Preferences

Consistent Features of Revealed Preferences Approach

- Positive correlation between risk and benefits
- Voluntary risks always riskier for the same amount of benefit

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Revealed Preferences

Important Drawbacks of Revealed Preferences Approach

- Assumes past behavior is valid indication of present preferences
- Politically conservative
- Ignores distribution of risks & benefits
- May under weigh risks to which the market is sluggish

Expressed Preferences

Definition: If people say it is safe, then it is safe enough.

Expressed Preferences

- Advantages
  - Elicits current preferences
  - Citizen involvement
  - Considers all aspects of risk and benefits
- Disadvantages
  - complex issues for general population
  - well articulated preferences for new and complex issues may not be available

Natural Standards

Definition: A technology is safe if its risk are no greater than those accompanying the development of the human species.

Natural Standards

- Advantages
  - Avoids need to convert risks to dollars
  - Compatible with people's natural thinking
  - Avoids referring to small probabilities
- Disadvantages
  - New exposures are in addition to background levels
  - No historical tolerance to new chemicals
  - Limited use

Regulation Philosophies

- Count the bodies
- Engineering solutions (BAT)
- Uniform Risk/Equal Rights
- Cost-Benefit
- Delaney Approach

Current Federal Issues

- Risk and Regulation
- Cost-Benefit Analysis

Uncertainties in Life

"Remember to change your underwear — you never know when you'll be in an accident."

Your Mother

Questions

Next Lesson

Population

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