

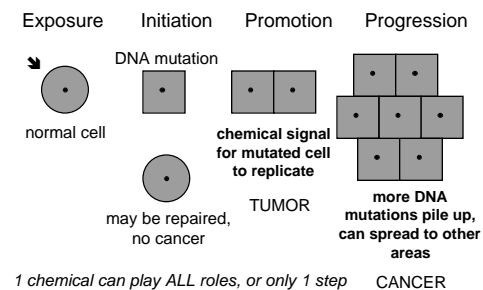
CVEN 4474/5474 Haz Waste Outline

- Carcinogens
 - How they work
 - Dose:Response
- Endocrine Disruptors
 - How do they work
 - Examples

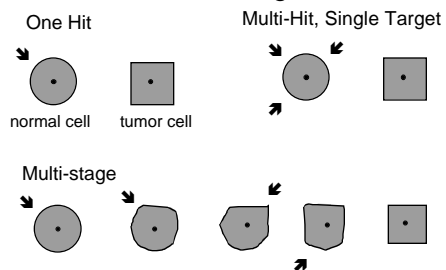
Carcinogens = ?

- Chemical (or radiation) which induces formation of tumors (aka "cancer")
 - 4 in 10 Americans will develop cancer in lifetime
 - 2 in 10 Americans will die from cancer
- 90% of cancers attributable to exposure to carcinogens (via lifestyle or involuntary)
10% of cancers attributable to genes/DNA
- No threshold ...even minute quantities can cause cancers
- Hard to quantify due to: latent period, low level effects, multiple exposures in daily life

How does cancer form?



Mechanistic Carcinogen Models



Finding chemicals that cause cancer

- Look at low incidences / high concs
- Tests:
 - Ames Test: bacteria, short-term gene mutation
 - Cheap, fast, easy
 - Mammalian assays: tissue samples, gene mutation
 - Short term animal studies (rats, mice, rabbits)
- Sensitivity: true carcinogens found?
- Specificity: inc. non-carcinogens?
- Predictive value: if test Y, does it?

Risk or probability of cancer =

$$\text{Chronic daily intake} \times \text{carcinogenic potency factor}$$

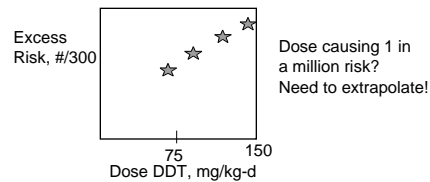
I, mg/kg-d CPF, kg-d/mg

The CPF is a slope factor
~ slope of probability vs Dose graph

Usually ADD effect of mixtures of chemicals if they target the same organs in the body

Example: "Mega Mouse" Study

- 2400 mice tested
- 8 doses of DDT in diet
- Looked for incidence of liver cancer



Extrapolated dose

Model	mg DDT/kg-d causing 1 in a million excess liver cancer
single hit	0.00021
multi-hit	0.013
multi-stage	0.00025
log-normal	0.68
log-log	0.0066
Weibul	0.05

All models similar fit to data, ...
~3 orders of magnitude difference in low dose estimation

More uncertainty....

- What is "safe" for a mouse?
- What is "safe" for a human?

EPA Carcinogen Classifications

- **A = human carcinogen**
–sufficient human epidemiological studies
- **B1 = highly probable human carcinogen**
–limited human data, strong animal data
- **B2 = low probable human carcinogen**
–inadequate human data, sufficient animal data
- **C = possible human carcinogen**
–No human data, limited animal data
- **D = not classified (inadequate data)**
- **E = non-carcinogen for humans**
–negative animal &/or human studies

Few "Class A" Carcinogens

- Arsenic
- Asbestos
- Aflatoxin B
- Benzene
- Benzidine
- Bis(chloromethyl)ether
- Chloromethyl methyl ether
- Chromium VI
- Nickel
- 2378-TCDD (dioxin)
- Vinyl Chloride
- Env. Tobacco Smoke (ETS)

- Cancer registries in U.S. track new diagnoses of cancers
–1995 1.2M people in US diagnosed with cancer
– # of cancer, but also pop. & older Amer.
–Can age adjust and population normalize
–Ex: 24% breast cancer in women in Mass. 1982-1990
- # of "possible" carcinogens in environment
–40 in drinking water
–60 released by industry into air (TRI)
–60 routinely used as pesticides

Where to find carcinogen data

- WEB-SITES
 - EPA's IRIS (www.epa.gov/iris)
 - ATSDR (www.atsdr.cdc.gov)
 - EXTOXNET (pesticides)
 - DOE (radionuclides)

use these sources to find data on chemical toxicity for your risk assessment projects

Example data for radionuclides

Slope factor

(lifetime excess total cancer risk per unit intake or exposure)

isotope	Lung clear class	GI Abs Factor	Ingest risk/pCi	Inhale risk/pCi	Extern risk/yr per pCi/g soil
U235	Yr	0.05	4.5 E-11	1.3E-8	2.6E-7
Rn 220	(gas)	--	--	1.9 E-13	1.9E-9
P32	D	0.8	6.1 E-12	2.9 E-12	0

Endocrine Disruptors

- Chemical disrupts hormone levels in the body or mimics hormones in the body
- “Our Stolen Future” Colburn, et al.
- Hormones regulate brain development, reproductive organs, blood sugar, etc.
- Example: estrogen mimics (PCBs, pesticides)
 - Decrease immune system
 - Change male/female characteristics
 - Decrease sperm counts/activity in humans
 - Cause cancer in reproductive organs
 - Linked to hyperactivity, clinical depression

Endocrine Disruptors (cont.)

- Dose:Response effect often a “bell curve”
 - Easy to have large errors in predicted effects if all doses of interest not tested
- VERY low doses (nanograms/L) can cause the adverse effects
- Effects may be manifested as carcinogenic and/or non-carcinogenic effects