ECTR

Lecture Slides

Lect. 3

Carcinogens

[Slides for 1st part of lecture are all taken from the figures in the reading, so are not included here]

CARCINOGENESIS

- 1 million cases per year of cancer
- 500,000 deaths per year

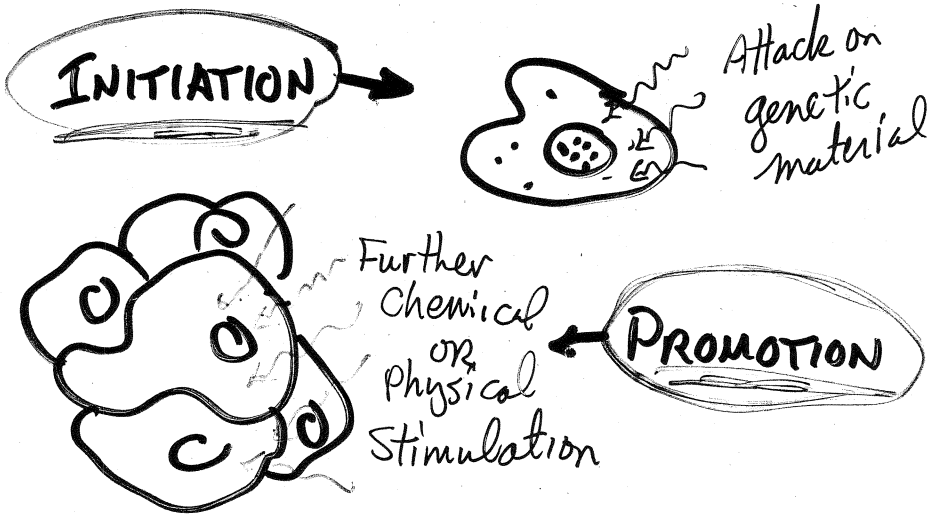
CHEMICAL INDUCTION OF CANCER

Two stages

INITIATION

↓

PROMOTION



PROBABILITY AND TOXICITY TESTING

TRIAL #

(0) 100 rats → Control (No Dose)

Result: No cancers

(1) 100 rats → Dose Level "A"

Result: 1 cancer 

RISK: $1/100 = 0.01 = 1\%$

(2) 100 rats → Repeat at Dose Level "A"

Result: 3 cancers 

RISK: $3/100$ IN THIS RUN

$4/200$ CUMULATIVELY $= 1/50 = 2\%$

(3) 100 rats → Repeat Dose Level "A"

Result: 0 cancers

RISK: $4/300$ CUMULATIVELY $= \frac{1}{75} = 1.33\%$

CONCLUSIONS

- With 200 rats (control + test) Can find it's roughly 1%
- with 300 rats we see its possibly 2%. So is 2% a more accurate number just because we used 50% more rats?
- with 400 rats we appear to "refine" our estimate back towards 1%.

→ Statistically our confidence increases

→ But can be difficult to really narrow it down.

BOTTOM LINE:

Animal studies detect risks down to the 1% to 10% level, at best.

REALITY:

- Effects can ONLY be seen if animals are given relatively enormous doses over ~all their lifespan.

- High doses may greatly exagerrate the PROMOTER effect over the INITIATOR effect. (High dose physically injures the organs, lowers natural resistance.

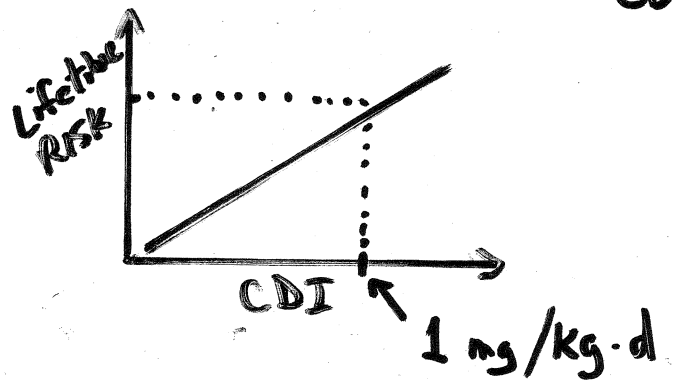
- Many human exposures are very LOW levels (1000-10,000 x lower than test)
  - OR -
  For fairly short periods
  (E.g., 5 yrs working in a pesticide plant out of a 70 yr lifespan.)

CARCINOGEN POTENCY OR SLOPE FACTOR

$$\text{Potency Factor (Slope factor)} = \frac{\text{Incremental Lifetime Cancer Risk}}{\text{Chronic Daily Intake (CDI)}}$$

(mg/kg·day)

P.F. = SLOPE OF DOSE-RESPONSE CURVE



Also can interpret P.F. as the **Lifetime Cancer risk associated with a CDI (dose) of 1 mg/kg·d**

HUMAN CANCER STUDIES

Basic Idea:

	WITH CANCER	WITHOUT CANCER
EXPOSED	a	b
NOT EXPOSED	c	d

Relative Risk: $\dfrac{\frac{a}{a+b}}{\frac{c}{c+d}}$ — "EXPOSED WHO GET CANCER" / "NOT EXPOSED WHO GET CANCER ANYWAY"

RR > 1.0 suggests exposure cause cancer

COMPLICATIONS:

- Smokers vs. Nonsmokers
- Men vs. Women vs. Children
- Workers vs. Nonworking population
- Confounding factors: Air pollution? Diet? Age? Race or ethnicity?

EXAMPLE FROM READING: (4.2) p. 141

Chlorinate drinking water
↳ May form small amts. of CHLOROFORM ($CHCl_3$)

SUPPOSE a 70 kg person drinks 2-L of H_2O per day for 70 yrs

$$\underline{CDI} = \frac{(0.10\ mg/L) \times (2\ L/day)}{70\ kg}$$

$$= 0.00286\ mg/kg\text{-}d$$

$$\underline{RISK} = CDI \times P.F.$$

$$= 0.000286 \times 6.1 \times 10^{-3} = 17.4 \times 10^{-6}$$

(17 EXCESS CANCERS PER MILLION PEOPLE)

$$\underline{\text{POPULATION IMPACT}} = \frac{\text{POPL'N} \times \text{RISK}}{\text{LIFETIME}}$$

$$= \left(\frac{500{,}000\ \text{people}}{}\right) \times \frac{17.4\ \text{Cancers}}{\text{million people}} \times \frac{1}{70\ yr} = 0.12\ \frac{\text{EXCESS CANCERS}}{\text{PER YR}}$$

BACKGROUND CANCERS:

$$(500{,}000) \times \frac{193\ \text{cancer/yr}}{100{,}000} = 965\ \frac{\text{cancers}}{yr}$$

BACKGROUND