EC+R
Lecture Slides
Lect. 3
Carcinogenesis

[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

Initiation

Further chemical or physical stimulation

Promotion

Attack on genetic material
CONCLUSIONS

- With 200 rats (control + test)
  Can find it's roughly 1%.

- With 300 rats we see it's 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 exaggerate 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.)

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**CARCINOGEN POTENCY OR SLOPE FACTOR**

\[
\text{Potency Factor} = \frac{\text{Incremental Lifetime Cancer Risk}}{\text{Chronic Daily Intake (CDI)}}
\]

\[
\text{P.F.} = \text{SLOPE OF DOSE-RESPONSE CURVE}
\]

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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:

<table>
<thead>
<tr>
<th></th>
<th>WITH CANCER</th>
<th>WITHOUT CANCER</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXPOSED</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>NOT EXPOSED</td>
<td>c</td>
<td>d</td>
</tr>
</tbody>
</table>

Relative Risk: \[
\frac{a}{a+b} = \text{"EXPOSED WHO GET CANCER"}
\]

\[
\frac{c}{c+d} = \text{"NOT EXPOSED WHO GET CANCER ANYWAY"}
\]

\[
RR > 1.0 \text{ suggests exposure cause cancer}
\]

Complications:
- Smokers vs. Non-smokers
- Men vs. Women vs. Children
- Workers vs. Non-working population
- Confounding factors: Air pollution?
  Diet? Age?
  Race or ethnicity?

Example from Reading (4.4) P.141

Chlorinate drinking water

\[
\text{May form small amounts of CHLOROFORM (CHCl}_3\text{)}
\]

Suppose a 70 kg person drinks 2 L of H₂O per day for 70 yrs

\[
\text{CDI} = \frac{(0.10 \text{ mg/L}) \times (2 \text{ L/day})}{70 \text{ kg}}
\]

\[
= 0.00286 \text{ mg/kg-d}
\]

\[
\text{RISK} = \text{CDI} \times \text{P.F.}
\]

\[
= 0.00286 \times 6.1 \times 10^{-3} = 1.74 \times 10^{-6}
\]

\[
\text{POPULATION IMPACT = POPLN \times RISK LIFETIME}
\]

\[
= (500,000 \text{ people}) \times \frac{17.4 \text{ cancers}}{\text{million people \times 70yr}} \times \frac{1}{0.12} \text{ excess CANCER AT PER YR}
\]

\[
\text{BACKGROUND CANCERS: (500,000) \times \frac{493 \text{ CANCER/yr}}{100,000} = 965 \text{ CANCERS PER YR}}
\]