Adult non-occupational pesticide exposure and cancer risk

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Non-occupational exposure

Evidence for non-occupational exposures and adult cancers for...
- Persistent organochlorine pesticides
- Home and garden pesticides
- Agricultural pesticides

Research needs; exposure assessment
GLOBAL PESTICIDE USE

- North America uses about 30% of the world total
- Europe uses about 27%
- Japan uses about 12%
- Approximately 31% is used in developing nations, including China
Pesticide Use in the United States
(U.S. Geological Survey Circular 1225; conventional pesticides only)
# U.S. home and garden pesticide use by pesticide class: 2000-2001

<table>
<thead>
<tr>
<th>Pesticide Class</th>
<th>Millions Pounds a.i.</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herbicides</td>
<td>62</td>
<td>69</td>
</tr>
<tr>
<td>Insecticides/Miticides</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td>Fungicides</td>
<td>11</td>
<td>12</td>
</tr>
</tbody>
</table>

Changes in pesticide use over time

- Organophosphates, carbamates, pyrethroids insecticides replaced organochlorines

- Currently (2001):
  - highest agric. use: glyphosate, atrazine
  - insecticide: malathion (#6)
  - highest non-ag use: 2,4-D, glyphosate
  - insecticide – diazinon (#4)
Sources of Pesticide Exposure - General population

Homeowner indoor pest control application
Homeowner lawn and garden application

Drift from agriculture, public land maintenance & insect control
Indoor air contamination at home, school, offices
Recreational areas, such as golf courses & parks
10% community water systems and 4% of rural wells had one or more pesticide or pesticide degradate (EPA)

Tap water in 27 of 29 cities tested contained 2-9 different pesticides (Env. Working Group)

14.1 million people routinely drink water contaminated with 5 herbicides tested (Env. Working Group)

Monitoring of public water supplies only required since late 1980s; herbicides/atrazine most commonly detected
Pesticides and Diet

- Dougherty et al., 2000 calculated average exposure to 30 pesticides

- Benchmark concentrations (for carcinogenic and noncarcinogenic effects) were exceeded for chlordane, DDT, dieldrin
  - Fish consumption accounted for large percent of food exposure

- Exposures to OP insecticides primarily from diet – reduce exposure with organic fruits/veg
  - Lu et al. 2006; Bradman et al, 2008
Pesticide Exposure

♦ Most occupational and environmental pesticide exposure and absorption is through skin

♦ Exposures through food and water, though common, are typically very low
  ♦ Organochlorine from dietary sources especially in the past

♦ “Exposure to pesticides by the largest number of persons probably occurs in and around the home” (Nigg et al., 1990)
Home and garden use

1990 EPA Home and Garden Pesticide Use Survey:
- 82% U.S. households use pesticides
- 66% treat primary living area 1+/year
- 22-33% use herbicides on yard or garden annually
- Application rate/acre for household lawns often greater than for agricultural land
Organochlorine Insecticides

- Widespread use mid-1940s to 1960s most banned now
- DDT, chlordane, lindane, aldrin, …
- Less acutely toxic than organophosphate insecticides
- Bioaccumulate, travels long distances in atmosphere, endocrine-disrupters
- Banned for concerns about health and environmental effects
Studies of DDT and Breast Cancer

- Many studies of DDT/DDE in serum or adipose
- DDT, other OCs have estrogenic activity
- Serum or adipose levels of DDE assoc. with risk in early case-control studies (Falck 1992; Wolff 1993; Dewailly 1994)
- Recent cohort, case-control studies in Mexico, Europe, and U.S. found no association
- Combined analysis of 5 U.S. studies (1400 cases, 1642 controls) Laden et al., 2001:

  \[ \text{OR (fifth quintile vs. first)} = 0.99 \ (0.77-1.27) \]
Studies of DDT and Breast Cancer

Issues (Snedeker; EHP 2001):

- Western women exposure (DDE) primarily through diet vs. occupational/environmental exposure to o,p’-DDT (most estrogenic form)

- Timing of exposure (in utero, prepuberty, etc)
  - Recent study (Cohn 2007) pos. association with exposure during puberty

- Multiple exposures and genetic polymorphisms often not evaluated
### Cyclodiene pesticides and breast cancer

<table>
<thead>
<tr>
<th>Chemical</th>
<th>No. Studies</th>
<th>Heterogeneity p-value</th>
<th>Pooled OR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldrin</td>
<td>2 studies</td>
<td>0.871</td>
<td>1.55 (1.00, 2.40)</td>
</tr>
<tr>
<td>Dieldrin</td>
<td>5 studies</td>
<td>0.144</td>
<td>1.19 (0.89, 1.61)</td>
</tr>
<tr>
<td>Oxychlordane</td>
<td>5 studies</td>
<td>0.080</td>
<td>0.77 (0.59, 1.02)</td>
</tr>
<tr>
<td>Trans-nonachlor</td>
<td>6 studies</td>
<td>0.636</td>
<td>0.86 (0.69, 1.09)</td>
</tr>
<tr>
<td>Cis-nonachlor</td>
<td>3 studies</td>
<td>0.384</td>
<td>1.10 (0.75, 1.63)</td>
</tr>
</tbody>
</table>

Khanjani et al, J Env Sci Health; 2007
Pesticides and Breast Cancer – Summary of the evidence

- DDT/DDE – Evidence does not support increased incidence
  - New study suggests that exposure in childhood increases risk (Cohn et al. 2007)
  - Evidence that it affects disease progression
- Other Organochlorines – Dieldrin and 13 other OC have been linked to risk, but evidence is inconsistent and mostly negative
- Atrazine – Linked to hormonal changes in wildlife, induces mammary gland tumors in some rats
- We do not know ... how long-term, lower level exposure from an early age is affecting breast cancer risk.
Endometrial cancer and OC pesticides

- Wiederpass et al, 2000:
  - 10 chlorinated pesticides including DDT, chlordane. No association with risk

- Sturgeon et al, 1998:
  - DDT, chlordane no assoc.
  - Non-significant elevated ORs for dieldrin
Pancreas cancer and OC pesticides

- Occupational studies show association with DDT

- 1 study of organochlorine levels in serum found no clear association (Hoppin et al, CEBP; 2000)
Testicular cancer and OC pesticides

- **Hardell EHP; 2003:** 61 cases, 58 controls:
  - Chlordane associated with increased risk

- **McGlynn JNCI; 2008:** 754 cases, 920 controls:
  - Chlordane Q4 vs. Q1
    - OR = 1.46, 95% CI = 1.07 - 2.00 P(trend) = .026
  - DDE Q4 vs Q1
    - OR = 1.71, 95% CI = 1.23-2.38 P(trend) = .0002
Home and garden pesticide use and risk of adult cancer
Exposure assessment methods
- Interviews

- Self-reported home and garden use
  - Pests treated for each residence over time
  - Issues of recall
  - Report pest treated not active ingredient
Exposure assessment methods—house dust

- Carpet dust samples from home:

  Specialized vacuum method showed good correlation with used vacuum bag

  *Colt et al, 2008*
## Self-reported pesticide use and breast cancer

*(Tietelbaum AJE; 2007)*

<table>
<thead>
<tr>
<th>Pest treated</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never used lawn/garden pesticides</td>
<td>1.0</td>
</tr>
<tr>
<td>Weeds</td>
<td>1.43 (1.17-1.75)</td>
</tr>
<tr>
<td>Lawn insects</td>
<td>1.48 (1.20-1.82)</td>
</tr>
<tr>
<td>Pests in garden</td>
<td>1.58 (1.24-2.01)</td>
</tr>
<tr>
<td>Insects/diseases of outdoor plants</td>
<td>1.54 (1.20-1.98)</td>
</tr>
<tr>
<td>Indoor plants</td>
<td>1.48 (1.08-2.02)</td>
</tr>
</tbody>
</table>
Case-control study of NHL
(L.A., Detroit, Seattle, Iowa)

♦ 1200 living cases; 1100 controls; ages 20-74

♦ Occupational, home/garden use of pesticides at each residence >2 years 1970 onwards

♦ Carpet dust collection to measure in-home exposure to persistent pesticides

♦ Serum levels of organochlorine pesticides, other chemicals (PCBs)
Lawn/garden herbicides and NHL

Hartge et al., CEBP; 2006

- Self-reported use of lawn/garden pesticides not associated with risk

- Dust levels of 2,4-D and dicamba not associated with risk

- No association among those with higher dust levels and higher reported
### Dust measurements and self-reported home pesticide use and adult NHL

Colt et al, CEBP; 2006

<table>
<thead>
<tr>
<th>α-chlordane in house dust</th>
<th>Termite treatment</th>
</tr>
</thead>
</table>
| Not detected              | No                | 1.0  | 1.1 (0.5-2.5)  
|                           | Yes               | 1.5 (1.0-2.3) | 3.8 (1.4-8.4)  

Q4
OR=1.3

Ever OR=1.3
Organochlorine pesticides and NHL

De Roos et al., Cancer Res; 2006

- Serum levels of oxychordane: OR per 10 ng/g lipid = 1.17 (0.94-1.46)

- No association with dieldrin, HCCH, heptachlor, DDT, DDE

- Non-significant elevations among those in 90th percentile of exposure for chlordane and DDT
Residential exposures to agricultural pesticides
Sources of Pesticide Exposure

Rural/agricultural populations

- Exposures to agricultural pesticides are likely to be intermediate between occupational groups and general population
  - Agricultural drift (primary, secondary)
  - Occupational “carry home” exposure
  - Pesticides & degradates in ground & surface water

- >50% of population in Iowa lives within distance (500 m) possibly affected by pesticide drift
  *(Ward et al, EHP; 2006)*
Environmental exposure to agricultural (non-persistent) pesticides and adult cancer

♦ Few *adult* cancers studied

♦ Residential proximity to cranberry bogs linked to brain cancer (Aschengrau 1996; AJPH), breast cancer (Brody EHP; 2004)

♦ Higher rates of lymphoma *in* agricultural counties of Michigan and prostate cancer in Northern Plains States (Rusiecki et al, 2006)

♦ *Studies lacked detailed exposure information*
Agricultural pesticides and adult cancer in California

Clary & Ritz; AJIM; 2003

Residence in zip codes with high use of:

1,3-dichloropropene, captafol, pentachloronitrobenzene, dieldrin had higher pancreas cancer mortality

Reynolds et al, EHP; 2005
Reynolds et al, Env Res; 2005

Residential proximity to agricultural pesticide use:

no evidence of increased rates for select individual pesticides or groups (probable carcinogens, mammary carcinogens..)
Assessing agricultural pesticide exposure

• **Biologic measures**
  - fat-soluble

• **Environmental measures**
  - exposure duration unknown

• **Pesticide use surveys**
  - state level
  - California: 1 square mile
  - drift <1/3 mile (500 m)
Can satellite imagery be used to identify populations potentially exposed to agricultural pesticides?

Ward et al, Env. Health Perspect; 2000

Popn <500 m crop fields: Nebraska – 28% Iowa – 58%

Ward et al, Env. Health Perspect; 2000
Does residential proximity to crop fields predict residential exposure?

- Crop maps from satellite images
- Dust samples - 11 crop herbicides
- GPS residences

Ward et al, EHP; 2006
Crop acreage and agricultural herbicide detections and concentrations

<table>
<thead>
<tr>
<th>Acres</th>
<th>#det/#ND</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5/24</td>
<td>1.0</td>
</tr>
<tr>
<td>1-200</td>
<td>10/48</td>
<td>1.2 (0.3-4.4)</td>
</tr>
<tr>
<td>201-300</td>
<td>5/3</td>
<td>7.2 (1.1-49)</td>
</tr>
<tr>
<td>&gt;300</td>
<td>12/4</td>
<td>7.4 (1.3-41)</td>
</tr>
</tbody>
</table>

**Concentration:**

Increase per 10 acres 1.05 (1.03-1.07)

*OR adjusted for pesticide exposed occupations*

Ward et al, EHP; 2006
California pesticide use reporting database (1 sq mi)

Section A

RESIDENCE

Section B

1,400 lbs - Methyl Bromide Applied to Grapes
Comparison of Exposure Classifications:

**Pesticide use data only**

- Beans
- Corn
- Grapes

- Residence

- All applications in Section - proportional to buffer area in the section

**Pesticide use linked to crop maps**

- Sugar Beets
- Grapes
- Beans
- Corn
- grapes
- corn

- Applications to crops in buffer - proportional to crop area in buffer

Nuckols et al; EHP, 2007
Predominate Wind

Wind Pattern

Hayes 1984
Soil type (erosion potential)

Pesticides and cancer

- Strength of the evidence depends on the quality of the studies
- Criteria: strength of the association, dose-response, consistency across studies, biologic plausibility
- Large individual-based studies with good exposure data; evaluate multiple exposures; genetic subgroups, polymorphisms
THANK YOU – QUESTIONS??