Agricultural Pesticides and Childhood Cancer

Peggy Reynolds, Ph.D.
Northern California Cancer Center
Exploring the Connection - Canadian Cancer Society Meeting
November 12-13, 2008
Outline

- Background
  - Childhood cancers
  - Evidence for pesticide associated risks
- California studies of agricultural pesticides
  - Exposures to children
  - Cancer risks
- Challenges
Age-Specific Cancer Rates

Age Group

Incidence

Mortality

Rate per 100,000

0

20-

40-

60-

80-

2000

1500

1000

500

0

2500

3000
## Five Most Common Cancers

<table>
<thead>
<tr>
<th>Adults</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td><strong>Women</strong></td>
</tr>
<tr>
<td>Prostate</td>
<td>Breast</td>
</tr>
<tr>
<td>Lung</td>
<td>Lung</td>
</tr>
<tr>
<td>Colon</td>
<td>Colon</td>
</tr>
<tr>
<td>NHL</td>
<td>Endometrium</td>
</tr>
<tr>
<td>Bladder</td>
<td>Ovary</td>
</tr>
</tbody>
</table>
Types of Childhood Cancer (ages 0-14)

- Leukemia: 35%
- Lymphoma: 9%
- CNS: 20%
- Retinoblastoma: 3%
- Carcinomas: 3%
- Osteosarcoma: 2%
- Wilms: 5%
- Germ cell: 5%
- All others: 18%

California, 1988-1994
Childhood Leukemias (0-14) Percent Distribution by Type

- ALL: 79%
- AML: 12%
- CML: 2%
- Other: 7%

Source: Cancer in California, 1988-1991
“Known” Risk Factors (for some leukemias)

- Ionizing radiation
- Chemotherapy agents
- Certain inherited genetic disorders such as Down syndrome and leukemia
“Suspected” Risk Factors

- Maternal age
- Some birth characteristics
- Socioeconomic status
- Environmental tobacco smoke
- Chemicals
- Viral agents
Suspected Environmental Agents

- Pesticides
- Electric and magnetic fields (EMF)
- Traffic-related exposures
Recent reviews concluded that multiple studies show increased risk.

Primarily case-control studies of home and garden pesticide use and parental occupational exposures.

- Virtually no information on residential proximity to agricultural exposures.

Studies limited by small numbers, nonspecific pesticide information and potential case-response bias.
McFarland cancer rate mystifies experts

Texas town’s bitter harvest from cancer

Town where cancer lives

DEADLY HARVEST

People who live and work where our food is grown suffer high rates of cancer and birth defects. The culprit seems to be the poisons that make our fruits and vegetables so appetizing.

Cancer Cluster Probe Focuses on Dozen Pesticides

Dread and death in McFarland, California
McFarland Investigation
1988-1996

- Interview Study
- Environmental Testing
- Child Health Screening
- Four County Study
- Monitoring for New Cases
Scientists have no answers for poisoned town

Cancer clues elusive
State abandons study of McFarland cluster

Cancer rate for children not unusual

Study: No increase in cases of cancer found

State Officials End Study Of McFarland Cancer Cluster

Bakersfield
State officials have ended a six-year study of a childhood cancer cluster in McFarland without finding any single cause for the cancer.

"We all had something that had to be found because we couldn't incarcerate whatever the cause was," Robert Speak, an environmental health specialist at the University of California at Berkeley said at Thursday.

"There's always something else that could be looked at," Speak added. "If not feel that it would be useful to invent further resources at this point."

The study has involved tests of McFarland's soil, air, water and radiation levels plus the homes of ill children.

Meanwhile, United Farm Workers, whose members led the study, Genia Chervin, said outside the meeting in Bakersfield, Chervin, who wants people use a table props house, alleged that there was a covering in the cancer study. No said a study of cancer rates in four San Joaquin Valley counties is flawed.
Background: Childhood Cancer and Pesticides

- Previous DHS cluster investigations in agricultural communities where pesticide use is a concern
- These studies lacked sufficient power to detect moderate increases in cancer rates
- Need to take a broader perspective on those concerns by conducting large scale studies of agricultural pesticide use
Ambient exposures are important
Assessing pesticide exposures in children

- Parental interviews and questionnaires
- Biological markers and biomonitoring
- Existing geographic and environmental data
Rationale for GIS Studies

- Interest in environmental risk factors
- Subjects unable to self-report environmental measures
- Need for:
  - Population-based information
  - Independent assessment of environmental exposures
  - Time-specific exposures
  - Individual risk factor information
  - Good epidemiologic study design
California GIS Studies

- Statewide ecologic
  - Patterns of exposure
  - Patterns of rates
  - Block group level
  - Residence at diagnosis
  - Pesticide applications 1 year prior to diagnosis

- Statewide case-control
  - Early childhood cancers (< age 5)
  - Controls from California births
  - Maternal residence at birth
  - Pesticide applications 9 months prior to birth

- Northern California Childhood Leukemia Study
  - Molecular epidemiology case-control field study
  - Multi-institutional collaborations
  - Residential history information to assess windows of vulnerability
California’s Pesticide Use Reporting System

- All agricultural pesticides
- Full use reporting began in 1991
- Considerable detail for pesticide applications:
  - location (township range section)
  - active ingredient
  - pounds applied
  - number of acres and date applied
  - crops
  - application method
Public Land Survey System
San Joaquin County
Environmental Health Investigations Branch
California Department of Health Services

14,986 - 106,662 (lbs)
6,218 - 14,986
2,693 - 6,218
739 - 2,693
0 - 739
No Pesticide Use Reported

Pesticide Use Reporting System
San Joaquin County

Environmental Health Investigations Branch
California Department of Health Services
Sources: PUR 1991-1994
GDT Dynamap 2000
Pesticide Groups Studied

- Probable or likely carcinogens (U.S. EPA Class B2), 19 pesticides
- Possible or suggestive carcinogens (U.S. EPA Class C), 37 pesticides
- Developmental or reproductive toxicants, 27 pesticides
- Genotoxic agents, 18 pesticides
Pesticide Selection – Individual Compounds

- Ranked pesticides by various hazard measures including:
  - Pounds of use
  - Toxicological Evidence – cancer class and potency
  - Exposure Potential – volatilization flux and persistence
## Annual Average Agricultural Pesticide Use

**California 1991-1994**

<table>
<thead>
<tr>
<th>Pesticide Group</th>
<th>Annual Average Used (lbs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Pesticides</td>
<td>159,399,100</td>
</tr>
<tr>
<td>Probable Carcinogens</td>
<td>12,643,173</td>
</tr>
<tr>
<td>Possible Carcinogens</td>
<td>9,972,335</td>
</tr>
</tbody>
</table>
What are the potential exposures to children from agricultural pesticide use?
Agricultural pesticide use by quartile of block group median family income.
POPULATION UNDER 15 IN RURAL BLOCK GROUPS WITH CLASS B PESTICIDE USE GREATER THAN 100 LBS/MI$^2$
PERCENT OF INCOME QUARTILE BY RACE IN RURAL BLOCK GROUPS WITH CLASS B PESTICIDE USE ABOVE 100 POUNDS/MI$^2$

- HISPANIC
- WHITE
- BLACK
- ASIAN/OTHER
### Distribution of High Pesticide Use Census
Block Groups by Toxicological Groups

<table>
<thead>
<tr>
<th>Pesticide Group</th>
<th>Block Groups(^a)</th>
<th>Children &lt;15 in 90(^{th}) Percentile (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probable Carcinogens</td>
<td>4,932</td>
<td>169,884</td>
</tr>
<tr>
<td>Possible Carcinogens</td>
<td>6,218</td>
<td>198,375</td>
</tr>
<tr>
<td>Genotoxics</td>
<td>7,505</td>
<td>261,333</td>
</tr>
<tr>
<td>Developmental/Reproductive Toxins</td>
<td>6,647</td>
<td>266,960</td>
</tr>
</tbody>
</table>

\(^a\) Number of block groups with >1 lb/mi\(^2\) use density for that pesticide group. Total block groups included in this study was 21,443.
Are childhood leukemia incidence rates elevated in areas of intensive agricultural pesticide use?
Environmental Health Investigations Branch
California Department of Health Services


- 6,044 - 40,879 (lbs/sq mi)
- 1,749 - 6,044
- 254 - 1,749
- 36 - 254
- 0 - 36
- No Pesticide Use Reported

Pesticide Use By Block Group
San Joaquin County

Census Block Groups - 1990
- 6,044 - 40,879 (lbs/sq mi)
- 1,749 - 6,044
- 254 - 1,749
- 36 - 254
- 0 - 36
- No Pesticide Use Reported

0 6 12 18 Miles

Environmental Health Investigations Branch
California Department of Health Services
Sources: PUR 1991-1994
GDT Dynamap 2000
Rate Ratios for Leukemia by Pesticide Groups

Probable Carcinogens

Possible Carcinogens

Dev/Repro Toxicants
Are children with leukemia more likely to have been born in areas of intensive agricultural pesticide use?
Estimating Nearby Pesticide Exposure

1. Select TRSs for the areas around case residences.

- Case # 1 Residence
  - T2N, R2E, sec1
  - T2N, R2E, sec10
  - T2N, R2E, sec19

- Case # 2 Residence
  - T2N, R2E, sec2
  - T2N, R2E, sec11
  - T2N, R2E, sec20
  - T2N, R2E, sec12
2. For each pesticide, summarize pounds applied by TRS.

<table>
<thead>
<tr>
<th>Pounds Applied/TRS</th>
<th>T2N,R2E,sec1</th>
<th>T2N,R2E,sec2</th>
<th>T2N,R2E,sec3</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 lbs.</td>
<td>0 lbs.</td>
<td>400 lbs.</td>
<td></td>
</tr>
<tr>
<td>100 lbs.</td>
<td>100 lbs.</td>
<td>300 lbs.</td>
<td></td>
</tr>
<tr>
<td>200 lbs.</td>
<td>200 lbs.</td>
<td>200 lbs.</td>
<td></td>
</tr>
<tr>
<td>300 lbs.</td>
<td>0 lbs.</td>
<td>300 lbs.</td>
<td></td>
</tr>
<tr>
<td>400 lbs.</td>
<td>0 lbs.</td>
<td>400 lbs.</td>
<td></td>
</tr>
<tr>
<td>0 lbs.</td>
<td>0 lbs.</td>
<td>0 lbs.</td>
<td></td>
</tr>
</tbody>
</table>
3. Using a GIS, create half-mile buffers around each residence.
Estimating Nearby Pesticide Exposure

4. Using a GIS, determine percent of each TRS within buffer areas.

Example:
25% of T2N,R2E,sec1 is in buffer area.
Estimating Nearby Pesticide Exposure

5. Sum the proportionally weighted pounds for all TRSs within buffer.

- 25% x 0 lbs.
- 13% x 0 lbs.
- 26% x 100 lbs.
- 5% x 100 lbs.
- 23% x 0 lbs.
- 10% x 0 lbs.
- 40% x 200 lbs.

26 lbs. + 85 lbs. = 111 lbs.
Estimating Nearby Pesticide Exposure

6. Divide by buffer area to obtain pounds applied per square mile, in buffer.

\[
\frac{26 \text{ lbs.}}{.8 \text{ mile}^2} = 33 \text{ lbs./mi.}^2
\]

\[
\frac{85 \text{ lbs.}}{.8 \text{ mile}^2} = 108 \text{ lbs./mi.}^2
\]
Estimating Nearby Pesticide Exposure

Case # 1 Residence: estimated 33 lbs./mi.$^2$ pesticides applied in buffer area

Case # 2 Residence: estimated 108 lbs./mi.$^2$ pesticides applied in buffer area
Odds Ratios* for Childhood Leukemia and Chemical Groups

*Compared to <1 lb/mi²
Odds Ratios for Childhood Leukemia and Individual Agents

*Compared to <1 lb/mi²*
Strengths

- Ability to evaluate specific toxicological groups of pesticides.
- Ability to quantify pesticide levels.
- Exposures not subject to response bias.
- Population-based.
- Good power to detect associations of interest.
Design Issue Limitations

- Timing of Exposure
- Measurement of Exposure
- Biologic Markers
- Homogeniety/Heterogeniety of Effect for:
  - Cancer subtypes
  - Population subgroups
- Covariates
Is living near agricultural pesticide use a risk factor for childhood leukemia?
Case-control study
- Cases diagnosed 1995-2009
- Matched controls selected from California birth registration files

In-home personal interview (in Spanish or English)

Household survey and dust sample collection for residential levels of pesticides and chemicals

Lifetime residential histories
NCCLS Study
Indoor Pesticide Exposures

Odds Ratio

3 mos b4  during  1st year  2nd year  3rd year  3 mos b4
preg.     preg.     -         -         -         preg. -
           age 3

Conditional logistic regression, adjusted for household income.

Ma, et al/Epidemiology 2001
1991-1994 Annual Average Pesticide Use

- 1999 Respondents
  - 8,189 - 847,991 lbs.
  - 2,884 - 8,189 lbs.
  - 537 - 2,884 lbs.
  - 33 - 537 lbs.
  - 0 - 33 lbs.

Bay Area Counties
Central Valley Counties

50 0 50 100 150 Miles
Exposure Periods for NCCLS GIS Study

- By time period:
  - In utero
    - By each trimester
  - First year of life
  - Two years before diagnosis

- Cumulative Average:
  - Pesticide use from birth to the reference date divided by exposure time
Model for Pesticide Exposure Assessment in the NCCLS

Self-reports
- Residential history
- Pesticide use at home
- Parental occupational history

Home dust samples

GIS-based attributes
Linkage to the Pesticide Use Registry, CA
Challenges of Epidemiologic Research

- Observational, not experimental
- Study populations vary
- Risk factors difficult to measure
- Disease latency
- Need to adjust for associated risk factors
- Statistical uncertainty
Challenges of Environmental Epidemiologic Research

- Exposures are ubiquitous
- Risk information is limited
  - Limited toxicology
  - Little chemical detail
  - Limited measurement of exposure
  - Little human health information
  - Formulations change
- Respondents cannot self-report
- Timing matters
  - preconception, in utero, early life, cumulative
- Susceptibility matters
  - genes, nutrition, other factors
Requires Transdisciplinary Efforts from:

- Epidemiologists
- Clinicians
- Geneticists
- Toxicologists
- Chemists
- Statisticians
- Geographers
- Health Educators
- Advocates
Limitations of case-control studies
- Subject to participation and recall bias
- Preclude ability to conduct prospective environmental exposure assessment

Limitations of ecologic studies
- Lack residential history information
- Lack information on other risk factors
Summary

- Exposure assessment the “achilles heel” of environmental epidemiology
- Existing environmental databases and GIS are valuable tools for assessing exposures
  - Provide an independent source of information on exposure
  - Validation of this approach with biological and environmental sampling can be useful in improving the quality of exposure assessment
  - Offer insights when integrated with other study designs
Summary

- High public interest in agricultural exposures and children’s health
- Evidence for reported household pesticide use and childhood cancer risk
- Evidence for agricultural pesticide exposures to children
  - Disproportionate to economically disadvantaged and Latino children
- Challenges for assessing exposures and cancer risk
- Need for precautionary approach to chemical use
The Children of Earlimart

6 cancer cases haunt tiny farming town

By Lisa Fujimoto and Lew Griswold

Monica Tovar perches on the edge of the examining table, letting the doctor listen through his stethoscope as she breathes. Two earrings dangle from each ear. A knit cap sits jauntily on her head, covering the thin wisps of dark hair beginning to grow back. Monica has leukemia, a sometimes fatal blood disease. That has made her, at age 14, something of an expert on cancer treatment.

"They draw blood to see how my white count is," she says, walking at Kern Medical Center in Bakersfield to learn whether her blood-cell count is high enough to allow her to receive chemotherapy that day.

"If it’s too low, I don’t get it." Monica found out in March 1989 that she has leukemia. She became the sixth child stricken with cancer at Earlimart, a southern Tulare County farming town of 3,000 that straddles Highway 99.

The six cases constitute so-called "cancer clusters," a term having broad public health significance in the San Joaquin Valley, where scientists have confirmed three childhood cancer clusters since 1983. No cause for the cancer clusters has been found, but some of the families of the stricken children are convinced pesticides are to blame.

The six Earlimart cases — a leukemia, a thyroid cancer, three leukemias and a lymphoma — were discovered between 1984 and 1989. One of the children, Jimmy Castillo, was 3 years old when he died in March 1990 of complications of leukemia. The surviving children are between ages 5 and 14.

A town the size of Earlimart could be expected to have two children with cancer in 10 years, a state health expert said. That

See Town/7E