Hyperexcitability

Delay closing of the sodium channels that open during depolarization

DDT
1873
1939
1948

ALDRIN
<table>
<thead>
<tr>
<th>Species</th>
<th>Location</th>
<th>Average Concentration of DDE in Eggs (ppm)</th>
<th>Reduction in Shell Thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peregrine falcon</td>
<td>Alaskan tundra (north slope)</td>
<td>889</td>
<td>-21.7%</td>
</tr>
<tr>
<td>Peregrine falcon</td>
<td>Central Alaska</td>
<td>673</td>
<td>-16.8%</td>
</tr>
<tr>
<td>Peregrine falcon</td>
<td>Aleutian Islands</td>
<td>167</td>
<td>-7.5%</td>
</tr>
<tr>
<td>Rough-legged hawk</td>
<td>Alaskan tundra (north slope)</td>
<td>22.5</td>
<td>-3.3%</td>
</tr>
<tr>
<td>Gyrfalcon</td>
<td>Seward Peninsular, Alaska</td>
<td>3.88</td>
<td>0</td>
</tr>
</tbody>
</table>
Persistence of chlorinated hydrocarbon insecticides in agricultural soils.

<table>
<thead>
<tr>
<th>Insecticide</th>
<th>Years Since Treatment</th>
<th>Percent Remaining</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldrin</td>
<td>14</td>
<td>40</td>
</tr>
<tr>
<td>Chlordane</td>
<td>14</td>
<td>40</td>
</tr>
<tr>
<td>Endrin</td>
<td>14</td>
<td>41</td>
</tr>
<tr>
<td>Heptachlor</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>Dilan</td>
<td>14</td>
<td>23</td>
</tr>
<tr>
<td>Isodrin</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>Benzene hexachloride</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>Toxaphene</td>
<td>14</td>
<td>45</td>
</tr>
<tr>
<td>Dieldrin</td>
<td>15</td>
<td>31</td>
</tr>
<tr>
<td>DDT</td>
<td>17</td>
<td>39</td>
</tr>
</tbody>
</table>
Association of DDT and DDE with Birth Weight and Length of Gestation in the Child


Organochlorine Pesticides and Male Genital Anomalies.

R. Bhatia et al., *Environ. Health Perspect.* 113: 220, 2005

Premature Births in California Sea Lions: Association with High Organochlorine Pollutant Residue Levels.

Death knell for organochlorines

- Effects on non-target species
- Insect resistance
- Chemical stability: persistence in the environment
Currently Available Agents for Mosquito Control

**ADULTICIDES**

- Pyrethrins
- Cholinesterase Inhibitors

**LARVICIDE**

*Bacillus thuringensis*
PYRETHROIDS

Organic compounds obtained from chrysanthemum flowers and other plants

Cause hyperexcitability of the nervous system by delaying closing of the sodium channel

Are readily degraded and are non-persistent in the environment
Pyrethroids

(Z)-(1R)-cis-acid

Permethrin

(Z)-(1S)-cis-acid

Bifenthrin

(S)-alcohol (1R)-cis-acid

Deltamethrin
Acetylcholinesterase Inhibitors

Organophosphates

- Malathion

Carbamates

- Propoxur (Baygon)
Bacillus thuringensis
DO THEY WORK?

DO THEY LOWER THE RISK OF DISEASE?

DO THEY ALLEVIATE NUISANCE?

WHAT DO YOU MEASURE?
Summer of 1975
Manitoba Clean Environment Commission

Public Hearings: 7 full days

The issue: to consider the request from the City of Winnipeg Mosquito Abatement Dept. for permission to fog in residential areas.

Presentations from
the City of Winnipeg
pesticide industry reps
scientists
concerned citizens
politicians
“It is the recommendation of the Manitoba Environment Control Branch that the City of Winnipeg’s proposal to fog in residential areas be rejected until they can provide the Clean Environment Commission with sufficient data to show that fogging is of benefit in reducing mosquito populations to satisfactory levels, and that such benefits outweigh any adverse environmental effects which may occur.”

(July 30, 1975)
Medical Emergency
Absence of Evidence for Effectiveness of Adulticiding

- Municipal Board of Man. 1974
- Alberta Environ. Conserv. Author. 1974
- Man. Environ. Control Branch 1975
- MN Environ. Control Citizens Assoc. 1977
- Gov. Perpich of MN - - Expert Panel 1984
- Symp. Mosquito Control, MN Acad. Sci. 1985
- Dr. A.J. Thorsteinson
Absence of impact of aerial malathion treatment on Aedes aegypti during a dengue outbreak in Kingston, Jamaica.

Ministry of Health, Kingston, Jamaica

“… during the 5-year period, 1980-84 malathion applied by Fog Generators was not effective against Aedes aegypti. “

“… the seasonal variation of mosquitoes was inverse to that of reported dengue incidence.”
FOR WIDELY DISPERSED AGENTS SUCH AS DIELDRIN AND DDT, TO WHICH THE POPULATION-AT-LARGE IS GENERALLY AND UBIQUITOUSLY EXPOSED, HUMAN EXPERIENCE IS UNLIKELY TO PROVIDE ANY MEANINGFUL INDICATION OF SAFETY OR HAZARD.

( S. Epstein)
Adverse Effects

Current Dogma

Malathion is much less toxic to humans than to insects.

Malathion is registered by the Federal Government and when used properly is safe and effective.
<table>
<thead>
<tr>
<th>Compound</th>
<th>Structure</th>
<th>LD50 in rats</th>
<th>oral</th>
<th>dermal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mevinphos</td>
<td>[(C_2H_5O)_2-P-O-P-(OC_2H_5)_2]</td>
<td>1.1</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td>Dichlorvos</td>
<td>[(CH_3O)_2-P-O-CH=CCl_2]</td>
<td>80</td>
<td>107</td>
<td></td>
</tr>
<tr>
<td>Malathion</td>
<td>[(CH_3O)_2-P-CH=COOC_2H_5] [CH_2COOC_2H_5]</td>
<td>1375</td>
<td>4400</td>
<td></td>
</tr>
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</table>
Acute Toxicity

*Organophosphate poisoning*

- **Muscarinic**
  - increased secretions and sweating
  - abdominal cramps, defecation
  - bradycardia to heart block
  - urination
  - miosis

- **Nicotinic**
  - muscular weakness, twitching
  - dyspnea, cyanosis
  - increased blood pressure
  - pallor

- **Central nervous system**
  - anxiety, restlessness, headache, apathy, confusion, slurred speech, ataxia, convulsions
Acute Toxicity

“Using U.S. Poison Control Center records to identify bystander pesticide exposures: a one-year surveillance of four southeastern states.”


“The exposed persons were seen in a health care facility. The most implicated substance was malathion (30.4%), while 19.6% did not know the exposure substance.”
Acute Toxicity

“Malathion Exposure Associated with Acute Renal Failure”


Individual spraying home interior
Acute Toxicity

IMPURITIES

“Impurities in Malathion Found to Disable the Body’s Natural Ability to Detoxify Malathion”

“The Toxicological Properties of Impurities in Malathion”

In Pakistan, 7500 sprayers, 2800 poisoned, 5 deaths
Isomalathion: formed during storage
Acute Toxicity

BREAKDOWN PRODUCTS


formation of malaoxon
Acute Toxicity

Individuals with atypical or deficiency in cholinesterase

- 1/2800 Canadians of European ancestry
  high sensitivity
- 3-4 % of Canadians
  intermediate sensitivity
- Cholinesterase deficiency
  liver disease, malnutrition, infection
Acute Toxicity

Local anecdotal effects of fogging/spraying

- Acute irritant reaction
- Fainting and incapacitation
- Menstrual disorders
- Convulsions of animal pets
- Flu-like symptoms
- Decrease in brain enzyme in fish
Epidemiological studies

Some Examples
Long-term Toxicity


Malathion, chlordane and 2,4-D were associated with increased risk.


The concentrations used are comparable to those found in blood following various non-lethal human exposures to pesticides.


These results showed that parathion and malathion increased PCNA and induced mutant p53 protein expression of MCF7 cells in comparison to controls.
Long-term Toxicity


“We concluded that NHL was associated with specific pesticides after adjustment for other independent predictors: malathion (OR, 1.83; 95% CI, 1.31-2.55).”
Long-term Toxicity


“…. Aspirin might have a contributory role. Malathion is another putative cofactor.”
Cost/benefit ratio of a 50-year mosquito abatement program

- **Cost**
  - Financial: $200,000 per single round of fogging
  - Health and environmental: unknown

- **Benefit**
  - Nuisance index: unknown
  - Disease risk: unknown
A first step towards a rational program of mosquito abatement

In response to a request by Governor Perpich the Minnesota Department of Health assembled a panel of experts from across the U.S.

This panel concluded that information about mosquitoes was scant in Minnesota and that considerable information would have to be generated before mosquito management could be seriously contemplated or evaluated.

Ethical Use of Animals

• Even the most primitive species are not to be subjected to potentially harmful procedures, unless a rigorously designed protocol justifies performing the procedure.

• The proposed procedure must satisfy the criterion of yielding useful data that can benefit mankind.