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## The Toxicology of Pesticides Used to Control Mosquitoes

A Case Study of the 2004 West Nile Virus Epidemic in Maricopa County, Arizona  
By Al Brown


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### RISK MANAGEMENT CASE STUDY

**Vector species present for WEE, SLE, WNV, Dengue, Yellow Fever, Zika and Chikungunya**

**CULEX SPP.**



**Aedes aegypti**



Source: Maricopa County Environmental Services Department; and ADHS 2021

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### 6000 Culex sites






Source: Maricopa County Environmental Services Department; 2005

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### Integrated Mosquito Management

- Maricopa County uses integrated mosquito management to control mosquitoes.
- This includes breeding site elimination, public education, application of larvicides, active disease surveillance network and use of adult mosquito control pesticides only if necessary.
- Maricopa County follows national mosquito control program guidance from CDC and other national organizations.

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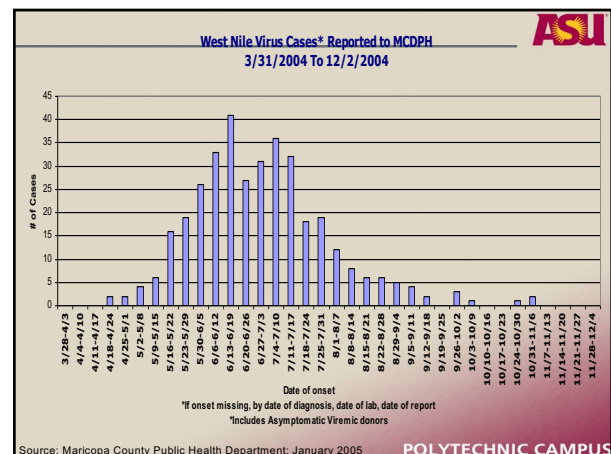
### Disease Severity Maricopa County Cases

<b>WNV Confirmed Cases:</b>	<b>355</b>
<b>WNV Confirmed Encephalitis:</b>	<b>112</b>
<b>WNV Confirmed Fevers:</b>	<b>91</b>
<b>WNV Confirmed Meningitis:</b>	<b>117</b>
<b>WNV Confirmed Symptomatic Viremic Donors:</b>	<b>22</b>
<b>WNV Confirmed Unknown:</b>	<b>13</b>

Based on MCPHD Case Classification Criteria

Source: Maricopa County Public Health Department; January 2005

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June 25, 2004  
 Johnny Dilone, Environmental Services (602) 506-6611

**FIRST HUMAN DEATH FROM WEST NILE VIRUS**  
**County Supervisors Pledge \$ 1 Million to "Fight the Bite"**

(Phoenix) - Maricopa County Supervisors' Chairman Andy Kanasak late this afternoon asked that \$1 million dollars be taken from the County Reserve Fund to be used in the fight against the West Nile Virus. The money will be used by the Maricopa County Department of Environmental Services to beef up fogging operations to kill mosquitoes.

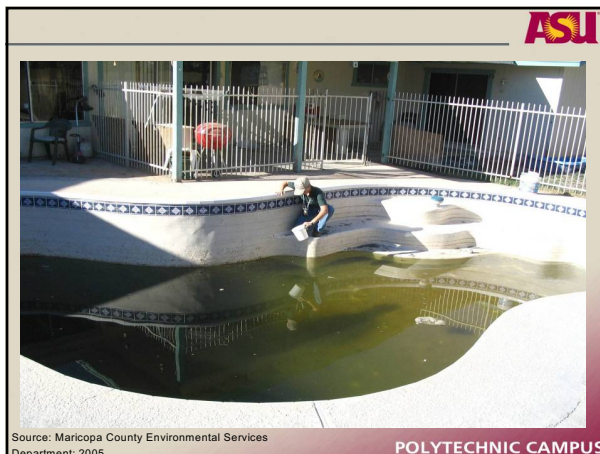
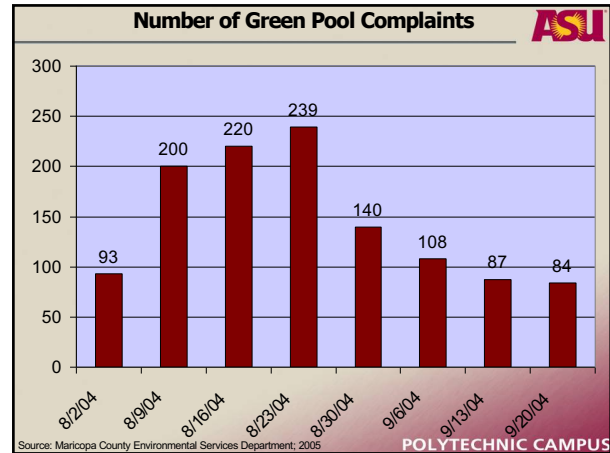
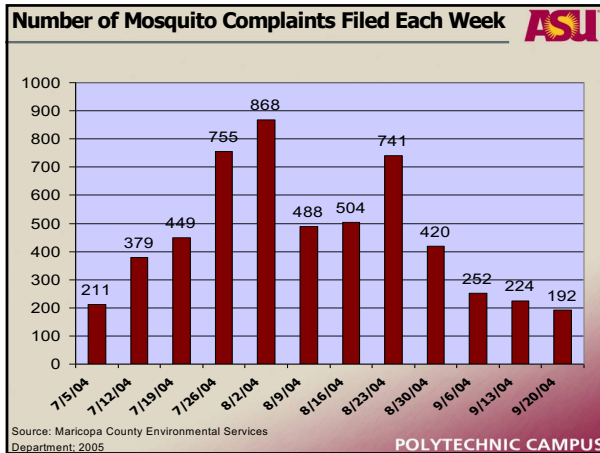
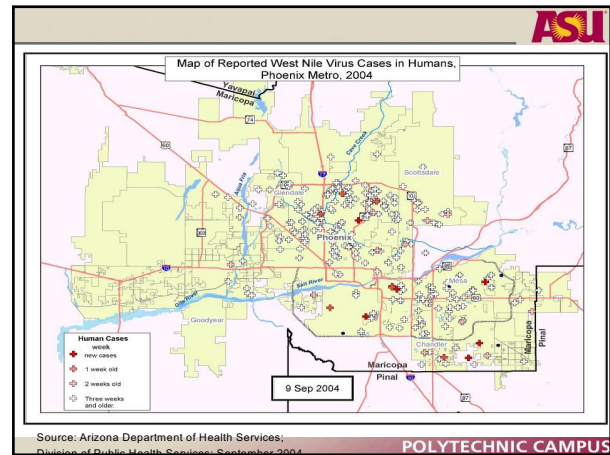
**United States House of Representatives**  
**J.D. Hayworth**  
 Listening to Arizona's Fifth District

**For immediate release: July 30, 2004**

CONTACT: Press Secretary Larry VanHousen (202) 225-2190

**Hayworth: Federal Funds Set Aside  
 For West Nile Emergencies**  
*Contacts CDC for help to stem Maricopa outbreak*

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**Arizona Department of Health Services**

**Office of the Director**  
 150 N. 18th Avenue, Suite 500  
 Phoenix, Arizona 85007-3247  
 (602) 542-1025  
 (602) 542-1062 FAX

**RECEIVED**  
**JUL 26 2004**  
 CATHY R. KERN, DIRECTOR  
 MCHS  
 DIRECTOR'S OFFICE

ARIZONA DEPARTMENT OF HEALTH SERVICES  
 ADMINISTRATIVE ORDER 2004-01  
 (Emergency Measures for West Nile virus)

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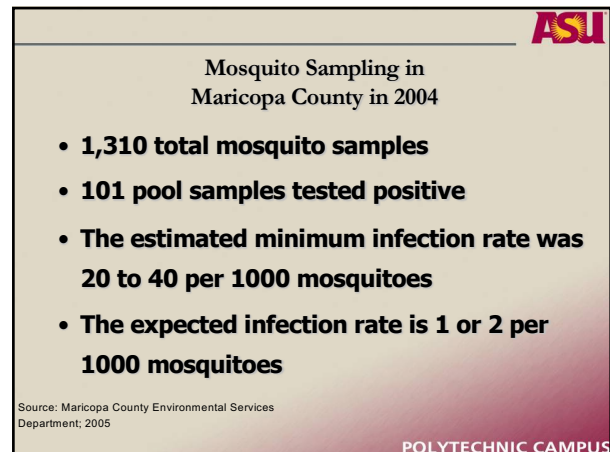
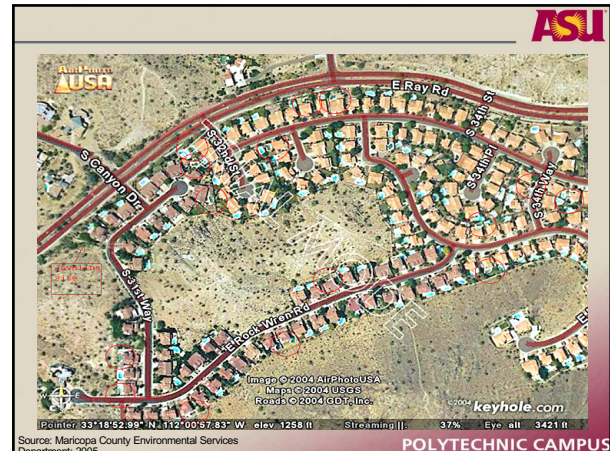
**West Nile Virus**  
 What is WNV? | How WNV spreads | Reducing the risks | Special Report

**Pools fueling West Nile in Phoenix**

Tuesday, August 17, 2004 Pooled: 3:49 PM EDT (1945 GMT)

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### Pesticides Evaluated for Adult Mosquito Control

- Malathion (organophosphate)
- Resmethrin (synthetic pyrethroid)
- Phenothrin (synthetic pyrethroid)
- Permethrin (synthetic pyrethroid)

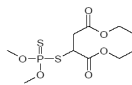
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### MALATHION

- Malathion inhibits acetylcholinesterase in humans and insects
- Cholinergic poisoning in humans causes a range of symptoms from headache, drowsiness, difficulty breathing, cardiac arrhythmias, confusion, coma, seizures and paralysis
- Malathion oxidizes in air to a more potent oxon analogue

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Table 4-1. Chemical Identity of Malathion

Characteristic	Information	Reference
CAS Nomenclature	Diethyl[(dimethoxyphosphinothioyl)thio]butanedioate	CAS 2001
Common name	Malathion	Howard and Neal 1992
Synonym(s)	1,2-Di[(ethoxycarbonyl)ethyl] O, O-dimethyl phosphorodithioate	Howard and Neal 1992
Registered trade name(s)	Cekumal Fyfanon® Malixol® Maltox®	Farm Chemicals Handbook 2000 Howard and Neal 1992 Farm Chemicals Handbook 2000 Howard and Neal 1992
Chemical formula	C <sub>10</sub> H <sub>16</sub> O <sub>6</sub> PS <sub>2</sub>	Howard and Neal 1992
Chemical structure		

Source: Toxicological Profile for Malathion; CDC/ATSDR, September 2003

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### Toxicity Guidance

#### Minimal Risk Level

An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse **non-cancer** health effects.

ATSDR uses the no observed adverse effect level/uncertainty factor (NOAEL/UF) approach to derive MRLs for hazardous substances. They are set below levels that might cause adverse health effects in the most sensitive population.

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### Toxicity Standards and Guidance

- Recommended Exposure Limit (REL) = NIOSH (National Institute for Safety and Occupational Health) time weighted average concentration for up to a 10-hour workday in a 40 – hour work week.
- Reference Concentration (RfC) = An estimate of a continuous **inhalation** exposure to the human population that is likely to be without an appreciable risk of deleterious **non-cancer** effects during a lifetime. RfC is expressed in mg/m<sup>3</sup> or ppm.

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### Toxicity Standards and Guidance

- Reference Dose (RfD) = An estimate of the daily exposure to the human population to a potential hazard that is likely to be without deleterious effects over a **lifetime**. The RfD is operationally derived from the NOAEL from human and animal studies. **RfDs are not applicable to cancer effects.**

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Table 2. Regulatory Standards and Guidance Values for Malathion		
Standard/Guidance	Value	Reference
Clean Water Act Maximum Contaminant Level(MCL)/Maximum Contaminant Level Goal(MCLG)	N/A	EPA 2002
Safe Drinking Water Act: 1- and 10-day Health Advisories (Child)	0.2 mg/L	EPA 2002
Reference Dose (RfD)	0.02 mg/kg/day	EPA 2002
Safe Drinking Water Act: Drinking Water Equivalent Level (DWEL)	0.7 mg/L	EPA 2002
Safe Drinking Water Act: Lifetime Health Advisory	0.1 mg/L	EPA 2002
Occupational Standards: Occupational Safety and Health Administration Permissible Exposure Limit (PEL) 8-hour time-weighted average	15 mg/m <sup>3</sup> (skin)	OSHA 2003
National Institute for Occupational Safety and Health/Centers for Disease Control and Prevention (NIOSH/CDC) Recommended Exposure Limit (REL)	10 mg/m <sup>3</sup> (skin)	NIOSH 2003
NIOSH/CDC Immediately Dangerous to Life or Health	250 mg/m <sup>3</sup>	NIOSH 2003
ATSDR Oral Minimal Risk Level (MRL) Intermediate and Chronic	0.02 mg/kg/day	ATSDR 2001
ATSDR Inhalation MRL, Acute	0.2 mg/m <sup>3</sup>	ATSDR 2001
ATSDR Inhalation MRL, Intermediate	0.02 mg/m <sup>3</sup>	ATSDR 2001
Department of Transportation Reportable Quantity	100 pounds	DOT 2002
Environmental Protection Agency Reportable Quantity	10 pounds	ATSDR 2001

\* EPA is reviewing the information in an application for reregistration of malathion and may shortly modify the RfD and establish an RfC.

Toxicologic Information about Insecticides Used for Eradicating Mosquitoes; CDC/ATSDR, April 2005

## Malathion: Chronic Health Effects




There is no evidence that malathion affects the ability of humans to reproduce. There is **also no conclusive proof that malathion causes cancer in humans**, although some studies have found increased incidence of some cancers in people who are regularly exposed to pesticides, such as farmers and pesticide applicators. The International Agency for Research on Cancer (IARC) has determined that **malathion is unclassifiable as to carcinogenicity to humans**.

Source: Toxicological Profile for Malathion; CDC/ATSDR, September 2003

## Synthetic Pyrethroids

- Pyrethroids are synthetic esters derived from the naturally-occurring pyrethrins
- Pyrethroids are a complex mixture of isomers rather than a single pure compound
- Synthetic pyrethroids paralyze insects by prolonging the open phase of the voltage-gated sodium channels when a nerve cell is excited. Tremors and body weight changes were observed in lab animals.
- Household use of synthetic pyrethroids **can trigger an asthma attack** in humans.
- Undiluted product may cause skin irritation.

Table 4-2. Chemical Identity of Selected Pyrethroids<sup>a</sup>

Characteristic	Permethrin	Phenothrin	Resmethrin
Synonym(s) <sup>b</sup>	(3-Phenoxyphenyl)methyl-3-(2,2-dichlorophenyl)-2,2-dimethylcyclopropane-carboxylate	(3-Phenoxyphenyl)methyl-2,2-dimethyl-3-(2-methyl-1-propenyl)-cyclopropanecarboxylate	[5-Phenyl(methyl)-3-furanyl(methyl)-2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropane-carboxylate
Ratio of isomers	(1R, trans):(1R, cis):(1S, trans):(1S, cis)=3.2:3.2 <sup>c</sup>	Mixed isomers	20–30% (1RS)-cis-isomers 80–70% (1(RS)-trans-isomers)
Registered trade name(s)	Ambush, Assitrin, Cliper, Coopex, Corsair, Dragnet, Dragon, Kafil, Eksmin, Perkill, Pounce	Sumithrin	Synthrin, Chrysron
Chemical formula	C <sub>21</sub> H <sub>29</sub> Cl <sub>2</sub> O <sub>3</sub>	C <sub>22</sub> H <sub>26</sub> O <sub>3</sub>	C <sub>22</sub> H <sub>26</sub> O <sub>3</sub>
Chemical structure			

Source: Toxicological Profile for Pyrethrins and Pyrethroids; CDC/ATSDR, September 2003

## Synthetic Pyrethroids: Standards and Guidance

Table 2. Regulatory Standards and Guidance Values for Resmethrin

Standard/Guidance	Value	Reference
Environmental Protection Agency Reference Dose (RfD)	0.03 mg/kg/day	IRIS 2003

Table 2. Regulatory Standards and Guidance Values for Permethrin

Standard/Guidance	Value	Reference
World Health Organization (WHO) drinking water guideline	20 µg/L	WHO 2001
Food and Agriculture Organization/WHO accepted daily intake (ADI)	0.05 mg/kg	HSDB 2003
Environmental Protection Agency Reference Dose (RfD)	0.05 mg/kg/day	IRIS 2003

Table 2. Regulatory Standards and Guidance Values for Phenothrin

Standard/Guidance	Value	Reference
World Health Organization acceptable daily intake (ADI)	0-0.07 mg/kg	WHO 1990

Source: Toxicologic Information about Insecticides Used to Eradicate Mosquitoes; CDC/ATSDR, April 2005

## Toxicokinetics of Pyrethroids

- Pyrethroids are excreted in the urine, feces and breath
- Pyrethroids are broken down inside the body into metabolites
- High doses of pyrethroids results in build up in fatty tissues
- Some pyrethroids may be retained in the skin and hair for longer periods

Source: Toxicological Profile for Pyrethrins and Synthetic Pyrethroids; CDC/ATSDR, September 2003



### Pyrethroid Chronic Health Effects



- There is no evidence that pyrethroids cause birth defects in humans
- There is evidence from animal studies that pyrethroids might be capable of causing cancer in people. But the evidence comes from animals that ate very large amounts of pyrethroids for a lifetime.
- Pyrethrins are classified as **“likely to be a human carcinogen by the oral route”** \*
- Possible endocrine disrupter at high doses

\* Cancer Assessment Review Committee

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### EPA Toxicity Rating Scale



Toxicity Label	High Toxicity: Danger	Moderate Toxicity: Warning	Low Toxicity: Caution	Very Low Toxicity: Caution
Oral LD50	<50 mg/kg	50-500 mg/kg	500-5000 mg/kg	>5000 mg/kg
Dermal LD50	<200 mg/kg	200-2000mg/kg	2000-5000 mg/kg	>5000 mg/kg
Inhalation LD50	<0.05 mg/L	0.05-0.5 mg/L	0.5-2 mg/L	> 2 mg/L

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### Pesticide Comparisons Page 1



Pesticide	LD50 (oral)	Toxicity	Non-Target Species	Persistence (half life)
Malathion	1522-1945 mg/kg	Low	Aquatic invertebrates, fish, insects	1-8 days (UV resistant)
Resmethrin	1244-4240 mg/kg	Low	Aquatic invertebrates, fish, insects	12 days
Phenothrin	>5000 mg/kg	Very Low	Aquatic invertebrates, fish, insects	12 days
Permethrin	500-4000 mg/kg	Moderate	Aquatic invertebrates, fish, insects	12 days

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### Pesticide Comparisons Page 2



Pesticide	Cost (per gal)	Use Restrictions	Notes
Malathion	\$38 (100% active ingredient)	Surface water	Odor, under EPA review; maloxon formation; RfD=.02 mg/kg/d
Resmethrin	\$24.50 (2% active ingredient)	Surface water	Low odor RfD=.03 mg/kg/d
Phenothrin	\$44.00 (2% active ingredient)	none	No odor No RfD*
Permethrin	\$24.50 (2% active ingredient)	Surface water	Low odor RfD=.05 mg/kg/d

\* ADI – 0.07 mg/kg/d

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### Piperonyl Butoxide



- Piperonyl butoxide (PB is a synergist used to enhance the effectiveness of pyrethrin and pyrethroid insecticides.
- Toxicity of PB is “Low”
- PB has no known reproductive effects
- PB is a Group C **“possible human carcinogen”**
- PB has a short half life in the environment (4.3 days)
- PB is moderately toxic to fish and highly toxic to aquatic invertebrates

Source: National Pesticides Telecommunications Network; Piperonyl Butoxide General Fact sheet, November 2000

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### Other Ingredients



- White mineral oil is an adjuvant in the formulation of many pesticides
- White mineral oil has “Low” toxicity
- White mineral oil is not classifiable as a carcinogen
- White mineral oil is used in many food and cosmetic products

Source: Pesticide Action Network; 2004

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## Other Ingredients continued



- **Aromatic hydrocarbons are used as solvents in many pesticide products**
- **Toxicity is “Low”**
- **Not classifiable as a carcinogen**
- **Listed as a “Potentially Toxic Other Ingredient/High Priority for Testing” by EPA**

Source: EPA List of Inert (Other) Pesticide Ingredients; August, 2005  
Pesticide Action Network, 2004

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## Other Ingredients continued



- Glycol ethers are listed as .4% of the formulation of Anvil.
- There are hundreds of glycol ethers; some are very low toxicity, others have moderate toxicity
- The type of glycol ether present in Anvil was not disclosed by the manufacturer

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Surveillance For Pesticide Related Illness in Nine States,  
1999 – 2002 <sup>(1)</sup>



- **“When administered properly in a mosquito-control program, insecticides pose a low risk for acute, temporary health effects”**

(1) CDC, MMWR, Vol.52, N.27, July 11, 2003

Source: Maricopa County Environmental Services  
Department, 2005

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## Pesticide Facts



- **Anvil 10 – 10 is the preferred pesticide for adult mosquito control**
- **Least toxic pesticide registered for use to control mosquitoes**
- **Toxicity is far less than exposure to environmental tobacco smoke**
- **Degrades rapidly in sunlight**
- **Application rate is extremely low (.3 oz – .5 oz per acre)**
- **Active ingredient is used to control lice on humans at 80 times concentration**

Source: Maricopa County Environmental Services  
Department, 2005

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## Pesticide Safety Precautions



- **Always minimize exposure to any pesticide**
- **Know when applications will occur**
- **Stay indoors with windows closed during the actual spraying**
- **Always wash garden fruits and vegetables before eating**
- **Bring toys or pets inside when pesticides are applied**

Source: Maricopa County Environmental Services  
Department, 2005

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Comparing Risk of Pesticide Exposure  
to Risk of Becoming Infected with West Nile Virus



- **Risk of contracting a West Nile Virus infection during the summer of 2004 was  $8.6 \times 10^{-3}$  population**  
(Based on Arizona Department of Health Services Estimates)
- **Risk of experiencing an illness from mosquito control pesticides is  $2.0 \times 10^{-7}$**   
(Based on CDC/MMWR, Vol.52.No. 27, July 11, 2003)

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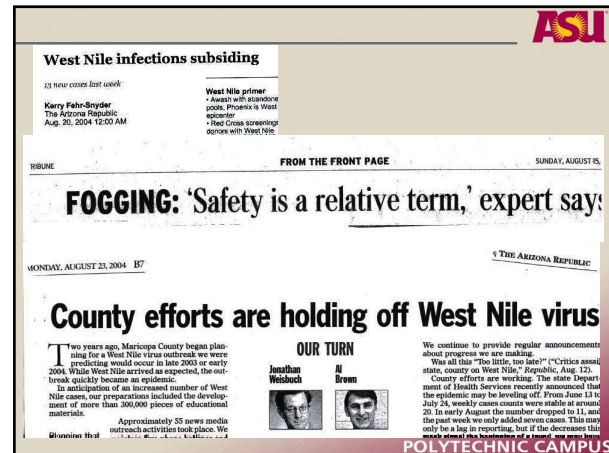


### Some Concerns Expressed by Residents



- The pesticides you are using cause heart disease, lung disease, impotence, decreased sperm count, kidney damage, thyroid damage, hormone changes, cancer, ADD, ADHD, early onset of menstruation, high blood pressure, seizures, depression, anxiety, autism, birth defects, bladder control issues, congestion, nausea, vomiting, diarrhea, fever, nosebleeds, asthma, anemia, rashes, swollen glands, muscle aches, brain damage and other maladies

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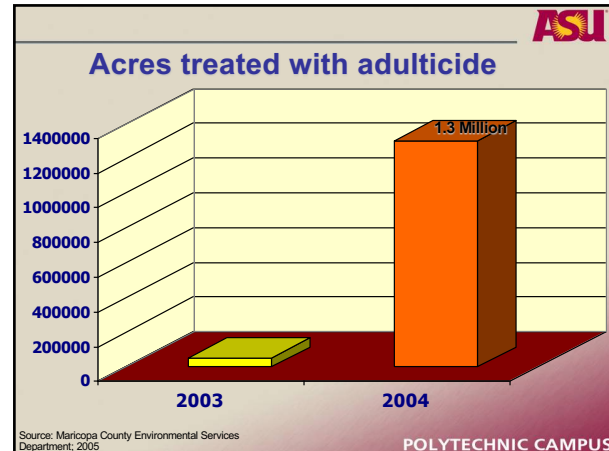
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### Some Concerns Expressed by Residents



- A helicopter sprayed my house with pesticides and I became ill the next day.
- I must leave the Phoenix area until the spraying stops because the pesticide drifts up to 22 miles from where it was applied.
- The spraying should be suspended while President Bush and Senator Kerry are here for their debates.
- If you ban all irrigation water usage, you won't have any mosquitoes to kill with your pesticides.
- Stop spraying my organic garden with pesticides.
- Government doesn't have authority to trespass on my property by spraying it with pesticides.

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### Is Fogging Effective?

#### Chandler, Arizona

Before Fogging

5-9-2004 1200 Cx. Tarsalis

After Fogging

6-3-2004 16 Cx. Tarsalis

**98.7% reduction**

Source: Maricopa County Environmental Services Department; 2005

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### Is Fogging Effective?

#### Scottsdale, Arizona

Before Fogging

8-5-2004 18 Cx.q, 2 Cx.Tarsalis

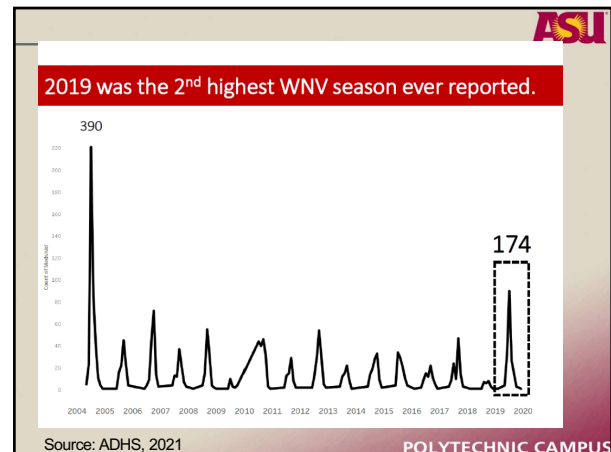
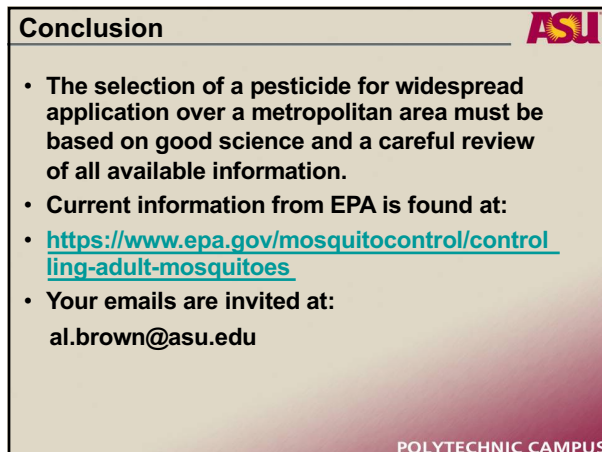
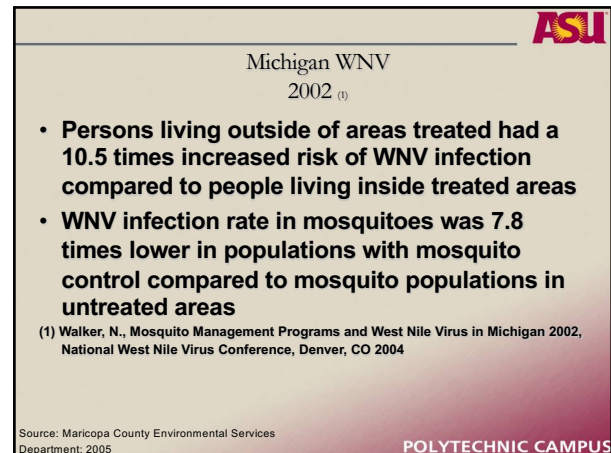
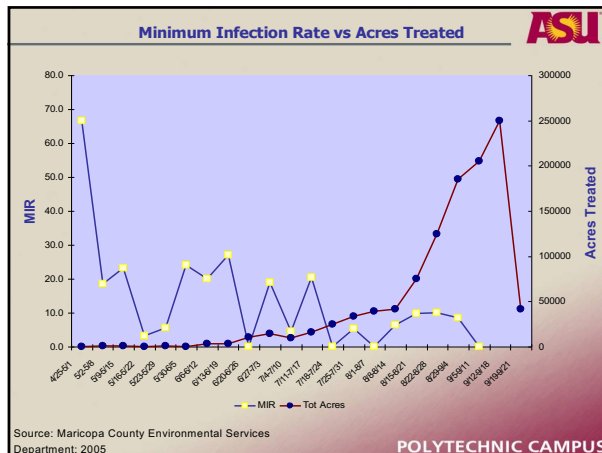
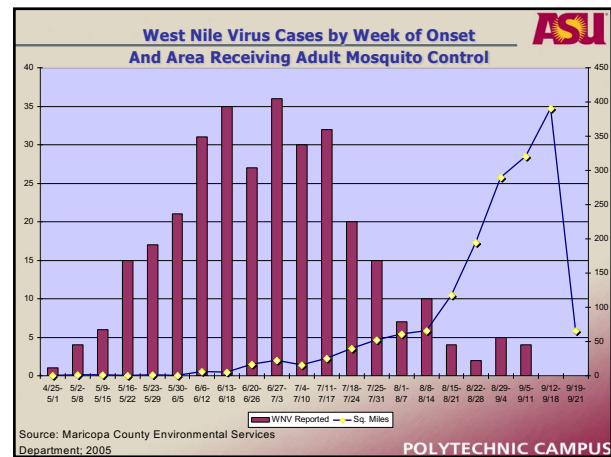
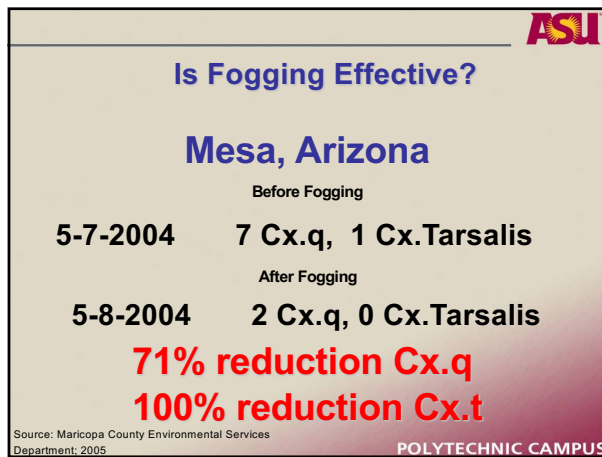
After Fogging

8-11-2004 2 Cx.q, 0 Cx.Tarsalis

**89% reduction Cx.q**  
**100% reduction Cx.t**

Source: Maricopa County Environmental Services Department; 2005

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## Vector abundance

$$\frac{\text{Number of mosquitoes of a particular species collected}}{\text{Number of trapping nights}}$$

For ex. 1,420 *Culex q.* collected during the summer

Useful as thresholds for mosquito control. However, high mosquito abundance may occur in the absence of virus or detectable virus amplification.


Source: ADHS, 2021

## Number of positive pools


A pool is a group of mosquitoes belonging to the same species.


Total number of WNV positive mosquito pools detected in a given surveillance location and period.

For ex. 23 *Culex q.* pools WNV positive during the summer




*Culex quinquefasciatus*  
WNV+





*Culex tarsalis*  
WNV+



Number of pools without a denominator limits the comparative value and the ability of this index to convey relative levels of WNV transmission activity.

Source: ADHS, 2021

## Vector index

$$\text{Average number of mosquitoes collected per trap night} \times \text{Proportion Infected}$$

N of Mosquitoes trapped	# Trap Nights	Avg Mosq/Night
80	2	80/2=40

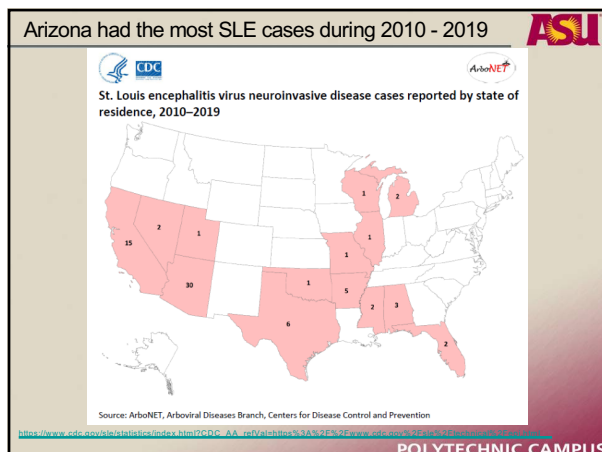
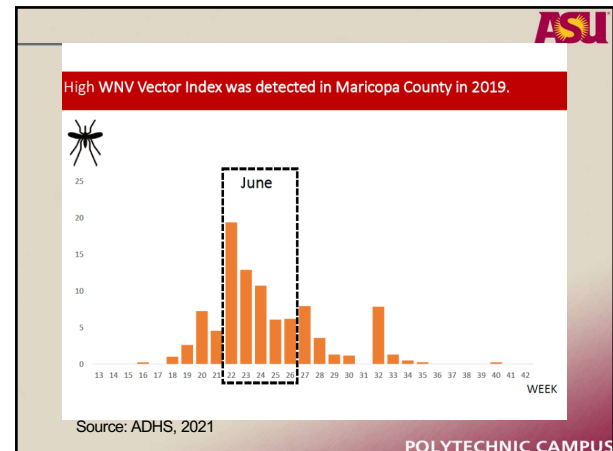
  

N of Positive Pools	N of Mosquitoes in pool tested	Proportion Infected
1	80	1/80=0.125

**Vector Index= 40 X 0.125= 0.5**

Increases in VI reflect increases in risk of human disease and have demonstrated significantly better predictive ability than estimates of vector abundance or infection rate alone.

Source: ADHS, 2021



### References for Mosquito Control Pesticides

- Toxicologic Information About Pesticides for West Nile Virus Control; CDC; April 2005
- Epidemic/Epizootic West Nile Virus in the United States: Guidelines for Surveillance, Prevention, and Control; 2003  
<http://www.cdc.gov/ncidod/dvbid/westnile/resources/wnvguidelines2003.pdf>
- Toxicological Profile for Pyrethroids and Pyrethroids; CDC, ATSDR; May 2021  
<https://www.cdc.gov/tsp/ToxProfiles/ToxProfiles.aspx?id=787&tid=153>
- National Pesticide Information Center <http://lnpic.orst.edu/wmv/>
- Joint Statement on Mosquito Control in the United States from the U.S. Environmental Protection Agency (EPA) and the U.S. Centers for Disease Control and Prevention (CDC) <https://www.epa.gov/mosquitocontrol/success-mosquito-control-integrated-approach>
- Malathion for Mosquito Control, <https://www.epa.gov/mosquitocontrol/success-mosquito-control-integrated-approach>
- Synthetic Pyrethroids For Mosquito Control, 2021 update  
<https://www.epa.gov/mosquitocontrol/permethrin-resmethrin-d-phenothrin-synthetic-pyrethroids-mosquito-control>
- Surveillance for Acute Insecticide-Related Illness Associated with Mosquito-Control Efforts --- Nine States, 1999--2002; July 11, 2003  
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5247a1.htm>
- Human Exposure to Mosquito-Control Pesticides --- Mississippi, North Carolina, and Virginia, 2002 and 2003  
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5421a1.htm>
- Maricopa County Environmental Services Department; Chemical Labels and MSDS, no longer provided online; must do a FOIA
- National Alliance for Informed Mosquito Management; February 23, 2005  
<http://www.beyondpesticides.org/mosquito/documents/aaimn.htm>



**ADHS Reference**

- Ruberto, Irene, 2021, Arboviral Diseases Surveillance in Arizona, ADHS Office of Infectious Disease Services, [Irene.Ruberto@azdhs.gov](mailto:Irene.Ruberto@azdhs.gov)
- <https://www.azdhs.gov/preparedness/epidemiology-disease-control/mosquito-borne/index.php>

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