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# EVALUATION OF EFFICACY AND HUMAN HEALTH RISK OF AERIAL ULTRA-LOW VOLUME APPLICATIONS OF PYRETHRINS AND PIPERONYL BUTOXIDE FOR ADULT MOSQUITO MANAGEMENT IN RESPONSE TO WEST NILE VIRUS ACTIVITY IN SACRAMENTO COUNTY, CALIFORNIA

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ABSTRACT. The Sacramento and Yolo Mosquito and Vector Control District (SYMVCD, also referred to as "the District") conducts surveillance and management of mosquitoes in Sacramento and Yolo counties in California. Following an increase in numbers and West Nile virus (WNV) infection rates of *Culex tarsalis* and *Culex pipiens*, the District decided on July 26, 2007, to conduct aerial applications of Evergreen® EC 60-6 (60% pyrethrins: 6% piperonyl butoxide) over approximately 215 km² in the north area of Sacramento County on the nights of July 30, July 31, and August 1, 2007. At the same time, the District received notification of the first human WNV case in the area. To evaluate the efficacy of the applications in decreasing mosquito abundance and infection rates, we conducted pre- and post-trapping inside and outside the spray zone and assessed human health risks from exposure to the insecticide applications. Results showed a significant decrease in abundance of both *Cx. tarsalis* and *Cx. pipiens*, and in the minimum infection rate of *Cx. tarsalis*. Human-health risks from exposure to the insecticide were below thresholds set by the US Environmental Protection Agency.

**KEY WORDS** West Nile virus, aerial spraying, insecticide, mosquito control, risk assessment

## INTRODUCTION

West Nile virus (WNV, family Flaviridae, genus *Flavivirus*) was first detected in the United States in 1999 in New York City, and reached California in the summer of 2003 (Reisen et al. 2004). In 2004, WNV amplified to epidemic levels and dispersed to all 58 counties in the state, and was associated with low-level transmission to humans and horses in Sacramento and Yolo counties that year (Armijos et al. 2005, Hom et al. 2005). In 2005, there was a severe outbreak in Sacramento County, with 177 human cases and 40 equine cases (Elnaiem et al. 2006).

The Sacramento and Yolo Mosquito and Vector Control District (SYMVCD, also referred to as "the District") conducts routine surveillance and management of mosquito populations in Sacramento and Yolo counties. The District monitors weekly mosquito abundance and West Nile, western equine encephalitis (WEE), and St. Louis encephalitis (SLE) viral infection. The District follows the California Mosquito-Borne Virus Surveillance and Response Plan (Kramer 2005) and its own Mosquito and Mosquito-Borne Disease Management Plan (SYMVCD 2005), and applies the principles of integrated pest management (IPM) in its program. When WNV reached epidemic levels in 2005 despite SYMVCD's intensive larviciding and public education efforts, the District intervened by aerially applying a formulation of pyrethrins and piperonyl butoxide (PBO) over an urban/suburban area in Sacramento County (Elnaiem et al. 2008), which most likely interrupted the WNV transmission cycle (Carney et al. 2008).

Although traditionally used in response to epidemics and as part of a sustainable public health program (Rose 2001), the application of pesticides often generates public concerns and controversy about the safety of these chemicals to people and the environment as well as the efficacy of such practice (Thier 2001, Roche 2002, Hodge and O'Connell 2005). A human health risk assessment conducted by Peterson et al. (2006) for truck-mounted ultra-low volume (ULV) applications of adulticides commonly used in mosquito management programs determined risks to be below levels established by the US Environmental Protection Agency (USEPA), which agrees with the current scientific weight of evidence (NYCDOH 2001, Karpati et al. 2004, Currier et al. 2005, O'Sullivan et al. 2005). The results from Peterson et al. (2006) indicated that potential health risks from WNV exceed risks from exposure to these pesticides when used at label rates to control adult mosquitoes. Their study used extremely conservative assumptions and estimated exposure after truck-mounted ULV applications as a worse-case scenario, used application rates greater than the ones used by SYMVCD, and therefore likely overestimated the exposure that would be seen for the application

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by the District. Schleier et al. (2009b) evaluated probabilistically the deterministic risk estimates presented by Peterson et al. (2006) and found them to be very conservative. Davis et al. (2007) evaluated ecological risks posed by adult mosquito management programs and concluded that risks to nontarget organisms from pesticides applied for adult mosquito management are low and not likely to exceed regulatory levels of concern.

Although vector control strategies and their effectiveness have generated concern in past years, there have been few published studies addressing the efficacy of these operations in reducing mosquito populations, infection rates, and virus transmission. Sacramento County experienced a WNV epidemic for the first time in 2005. Although the evaluation of the aerial adulticiding conducted during that year suggested interruption of transmission (Carney et al. 2008) and reduction of vector abundance (Elnaiem et al. 2008), some uncertainties were identified by SYMVCD staff to be addressed in future evaluations, particularly the absence of fixed locations for trapping mosquitoes before and after the applications, the small number of mosquito pools collected from those areas, and other confounding factors such as the effect of wind shadow at some of the locations.

In 2006, WNV reached epidemic levels in the cities of Davis and Woodland in Yolo County, and the SYMVCD, with the collaboration of the Center for Vectorborne Diseases at the University of California–Davis, monitored abundance and infection rates and conducted aerial applications of pyrethrins and PBO on the nights of August 8 and 9, 2006 (Macedo et al. 2007a, Nielsen et al. 2007). Analysis of data from 2005 and 2006 showed that the aerial applications could have been more successful in interrupting virus transmission to people if they had been conducted 1 wk or 2 wk before, when mosquito abundance and infection rates were higher (Macedo et al. 2008).

The first indication of active WNV transmission in the District in 2007 was the detection of WNV in a dead American crow on May 31. The first positive mosquito pool was obtained on July 4, 2007, in a pool of *Culex pipiens* L. West Nile virus continued to amplify during the month of July, and mosquito abundance and maximum likelihood estimates of minimum infection rates continued to be monitored. The District identified an area of approximately 215 $km^2$ in the north part of Sacramento County as higher risk and intensified all the aspects of its IPM program in an attempt to reduce mosquito populations. On the week of July 24, 2007, infection rates had reached 10.85 and 7.87 per 1,000 mosquitoes for *Culex tarsalis* Coquillett and *Cx. pipiens*, respectively. Following the guidelines of the California Mosquito-Borne Virus Surveillance and Response Plan (Kramer 2005) and its Mosquito and Mosquito-Borne Disease Management Plan (SYMVCD 2005), the District made the decision on July 26, 2007, to aerially apply pyrethrins and PBO (Evergreen EC-60-6®) over the area of concern. On the same day that this decision was made, the District received notification of the first human case in the area. The insecticide applications took place on the nights of July 30 and 31, and August 1, 2007. The objectives of this study were to 1) evaluate the efficacy of the aerial applications in reducing adult mosquito populations and infection rates of the two main species implicated in WNV transmission in Sacramento County and 2) assess human health risks for the aerial application of adulticide conducted in Sacramento County in 2007 in response to the WNV activity.

## MATERIALS AND METHODS

### Aerial applications and study area

The spray zone was a 215 $km^2$ area in northern Sacramento County, located in the Central Valley of California (Fig. 1). The insecticide Evergreen EC 60-6 (60% PBO and 6% pyrethins; McLaughlin Gormley King, Golden Valley, MN) was applied by a fixed-wing Piper Aztec and a Cessna 402 aircraft (VDCI/ADAPCO Vector Control Services, Greenville, MS) for three consecutive nights on July 30 and 31, and August 1, 2007. The application rate was 2.8 g/ha (0.0025 lb/ac) of pyrethins and 28 g/ha (0.025 lb/ac) of PBO. The release altitude was 91 m (300 ft), the wind speed ranged from 3.7 km/h to 18.5 km/h, and the temperature at the time of the applications ranged from 34°C to 36°C. Application start times ranged from 7:34 p.m. to 7:55 p.m. and application end times ranged from 9:20 p.m. to 9:51 p.m.

### Mosquito abundance

To evaluate the effect of the aerial applications on mosquito abundance, the District used encephalitis virus surveillance traps (EVS) baited with dry ice, herein referenced to as $CO_2$ traps (Rohe and Fall 1979), and gravid-female traps (Cummings 1992) to collect mosquitoes inside and outside of the aerial spray zone for 3 days before and 3 days after the application events. Trap collections were brought to the laboratory, where mosquitoes were anesthetized with triethylamine, identified to species and counted, and then frozen at −80°C for later virus testing. Three $CO_2$ traps and one gravid trap were placed at each of the 12 fixed sites in the aerial spray zone and six fixed sites in the untreated control zone (Fig. 1). Counts of females per trap-night were transformed by $\ln(y + 1)$ and expressed as

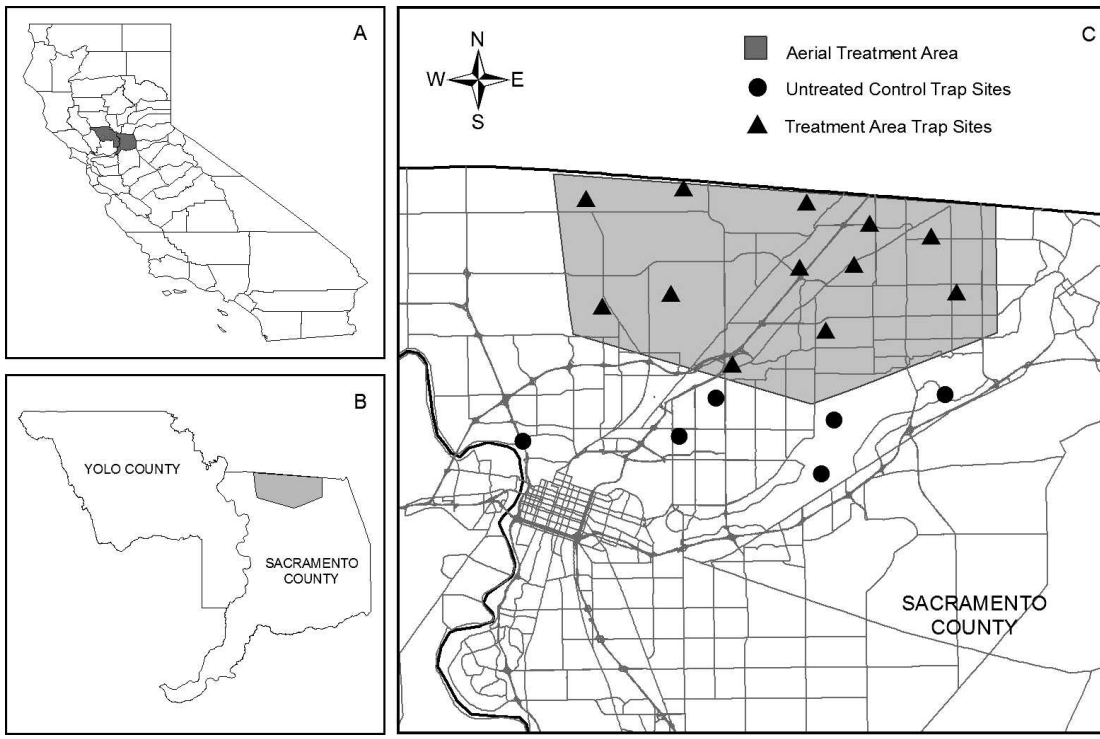


Fig. 1. Map of California showing (A) the location of Sacramento and Yolo counties, (B) the 2007 spray zone in north Sacramento, and (C) the locations of trapping sites used in the spray zone and untreated control area during 3 days before and 3 days after the aerial applications of pyrethrins and piperonyl butoxide in 2007.

geometric means (Reisen and Lothrop 1999), and analyzed by two-way analysis of variance (ANOVA) and paired *t*-tests (SAS, version 9.1, SAS Institute, Cary, NC). Percentage of reduction of *Cx. tarsalis* and *Cx. pipiens* abundance was estimated by the formula described by Mulla et al. (1971).

### West Nile virus infection rates

Mosquitoes from trapping conducted in the 18 fixed sites 3 days before and 3 days after the aerial applications, as well as from other traps set inside the spray zone during the week before and after the adulticide applications were collected and brought to the laboratory where they were then anesthetized with triethylamine, identified to species, pooled in groups of one to 50 females, frozen at −80°C, and tested for arboviral RNA (WN, SLE, and WEE viruses) by multiplex real-time reverse transcriptase–polymerase chain reaction (Shi et al. 2001), using WNV primers published previously (Lanciotti et al. 2000). Infection rates were calculated for the week before and the week after the aerial application events using bias-corrected maximum likelihood estimation (Biggerstaff 2006). In addition, percentage of reduction of minimum infection rates was estimated by the formula described by Mulla et al. (1971), which accounts for reductions or increases in the untreated areas.

### Sentinel cages

Sentinel mosquitoes were exposed within disposable bioassay cylindrical cardboard cages, 15 cm diam and 4.5 cm deep, with 14 × 18–mesh polyester screens on both vertical circular surfaces (modified from Townzen and Natvig 1973), with a hole in the cardboard for cotton pads moistened with 10% sugar water. One cage containing approximately 25 wild-caught adult *Cx. tarsalis* and another containing 25 wild-caught *Cx. pipiens* were placed at each of the 12 sites within the aerial spray zone and at the six control sites during each application. Cages were placed vertically at a 1-m height with a screened surface positioned to face the prevailing wind direction. Mosquito mortality was evaluated at the time of the placement of the cages (before the insecticide application), and at 1, 2, and 12 h after each application. Results were expressed as percentage of mortality.

### Human health risk assessment

Human health risk assessments had been previously conducted for truck-mounted applica-

tions of pyrethrins and PBO using greater application rates than the ones used by SYMVCD for adult mosquito control, and for a different application schedule (Peterson et al. 2006). We modified the risk assessments by Peterson et al. (2006) and Schleier et al. (2009b) to more accurately represent the application type, rate, and schedule used by SYMVCD in 2007. In addition to those modifications to the previous risk assessments, we incorporated more recent deposition data from Schleier et al. (2008). We estimated the human health risk from exposure to 3 days of aerial applications of pyrethrins and PBO at the rates specified above. To account for age-related differences, exposures were estimated for adult males and adult females (18–65 years of age), youth (10–12 years of age), children (5–6 years of age), toddlers (2–3 years of age), and infants (0.5–1.5 years of age).

*Toxicity and dose-response relationships:* Dose-response information for each compound was reviewed and endpoints were chosen based on acute and subchronic exposures. The toxicity thresholds used in this assessment were ingestion reference doses (RfD) established by the USEPA. Ingestion RfDs were based on the no-observed-adverse-effect level (NOAEL) with a 100-fold safety factor for intra- and interspecies extrapolation uncertainties. The acute oral RfD for pyrethrins and PBO are 0.07 and 6.3 mg/kg body weight (BW)/day, respectively (USEPA 2006a, 2006b).

*Risk characterization:* Total acute exposure to each active ingredient for each group was estimated by summing inhalation, dermal, hand-to-mouth, turf-dislodgeable, and ingestion exposure routes which are outlined below. The risk quotient (RQ) was calculated by dividing the total potential exposure for each group and chemical by its respective ingestion toxic endpoint value (RfD). The multi-route exposure was compared to the ingestion RfD because it provided a conservative endpoint, which is based on the most sensitive NOAEL. Estimated RQs were compared to a RQ level of concern (LOC), which is set by the USEPA or other regulatory agencies to determine if regulatory action is needed. The RQ LOC used in the assessment was 1.0. An RQ $>1.0$ means that the estimated exposure was greater than the relevant RfD.

*Probabilistic analysis:* Monte Carlo simulation (Crystal Ball® 7.3; Decisioneering, Denver, CO) was used to generate the exposures and RQs. Probabilities of occurrence of RQ values were determined by incorporating sampling from the statistical distribution of each input variable used to calculate the RQs. Each of the input variables was sampled so that its distribution shape was reproduced. Then, the variability for each input was propagated into the output of the model so that the model output reflected the probability of values that could occur. This was performed by using 20,000 iterations with the assumptions outlined below and in Table 1. Respiratory rate, BW, percentage of surface area of two hands, air concentrations, and spray deposition were truncated at zero because it is not possible for these quantities to have negative values.

*Environmental concentrations:* We used the environmental concentration data from Schleier et al. (2008) at ground level using the same application rates listed above (see Schleier et al. 2008 for details of the applications). To model the deposition of pyrethrins and PBO onto surfaces, we created distributions using concentrations measured 1 h and 12 h after application because the concentrations at these times were not significantly different (Schleier et al. 2008). Distributions for deposition onto surfaces were chosen based on the Anderson–Darling goodness-of-fit test, which for non-normalized data weights the differences between two distributions at their tails (Pettitt 1977, Oracle 2007). The distribution fit of the environmental concentration data for PBO was log-normal with a mean 0.01 $\mu g/cm^2$ and a standard deviation of 0.01. To model air concentrations of PBO we assumed the same amount that deposited on the ground would be available in 1 $m^3$ of air. We used the same distribution for air concentrations as we did for ground deposition. Schleier et al. (2008) did not detect any pyrethrins during their study; therefore we modeled deposition and air concentrations using the same assumptions as for PBO, scaling the distributions based on the application rate. Pyrethrins were applied at an application rate 10% of that for PBO.

*Acute exposure:* We assumed that acute multi-route exposures immediately after a single-spray event were limited to 24 h. Routes of insecticide exposure to each group were inhalation, dermal, and dietary and non-dietary ingestion. Assumptions of body weight, respiration rate, and frequency of hand-to-mouth activity are presented in Table 1.

Because the data from Schleier et al. (2008) demonstrated that the inhalation exposure is most likely limited to 1 h, we assumed that each group would be outside when the aerial spray began and that the duration of the exposure was 1 h. Instead of using modeled environmental concentrations we incorporated the deposition rates of Schleier et al. (2008). The exposure modeling assumptions for dermal, hand-to-mouth, and turf-dislodgeable residues follow the assumptions of Schleier et al. (2009b), except actual environmental concentrations were used instead of modeled environmental concentrations. The modifications to inhalation and ingestion exposure are outlined below.

Table 1. Assumptions for body weight, respiratory rate, and frequency of hand-to-mouth activity for each group assessed.

| Input Variables | Group | Parameter[1] | Values | Units | Distribution | Source |
|---|---|---|---|---|---|---|
| Body weight | Adult males[2] | Mean | 78.65 | kg | Log-normal (truncated) | Portier et al. (2007) |
| | | SD | 13.23 | | | |
| | Adult females[3] | Mean | 65.47 | kg | | |
| | | SD | 13.77 | | | |
| | Youth[4] | Mean | 36.16 | kg | | |
| | | SD | 7.12 | | | |
| | Children[5] | Mean | 19.67 | kg | | |
| | | SD | 2.81 | | | |
| | Toddlers[6] | Mean | 13.27 | kg | | |
| | | SD | 1.62 | | | |
| | Infants[7] | Mean | 9.1 | kg | | |
| | | SD | 1.24 | | | |
| Respiratory rate | Adult males | Mean | 17.53 | $m^3$/day | Log-normal (truncated) | Brochu et al. (2006) |
| | | SD | 2.8 | | | |
| | Adult females | Mean | 13.78 | $m^3$/day | | |
| | | SD | 2.1 | | | |
| | Youth | Mean | 11.3 | $m^3$/day | | |
| | | SD | 2.14 | | | |
| | Children | Mean | 7.74 | $m^3$/day | | |
| | | SD | 1.04 | | | |
| | Toddlers | Mean | 5.03 | $m^3$/day | | |
| | | SD | 0.94 | | | |
| | Infants | Mean | 3.72 | $m^3$/day | | |
| | | SD | 0.81 | | | |
| Hand-to-mouth frequency | Toddlers | Location | 5.3 | events/h | Weibull (truncated) | Xue et al. (2007) |
| | | Scale | 3.41 | | | |
| | | Shape | 0.56 | | | |
| | Infants | Location | 14.5 | events/h | | |
| | | Scale | 15.98 | | | |
| | | Shape | 1.39 | | | |

[1] SD = standard deviation.
[2] 18–65 years of age.
[3] 18–65 years of age.
[4] 10–12 years of age.
[5] 5–6 years of age.
[6] 2–3 years of age.
[7] 0.5–1.5 years of age.

Inhalation exposure was estimated by

$$PE_{Inhalation} = (AEC \times RR \times D)/BW \quad (1)$$

where $PE_{Inhalation}$ is potential exposure from inhalation (mg/kg BW), AEC is actual environmental air concentrations (μg/$m^3$), RR is respiratory rate for each group ($m^3$/h), D is duration of exposure, and BW is body weight (kg) for each group (Table 1).

For acute ingestion exposure from tomatoes that were exposed to the pesticide, we assumed that all foods containing tomatoes eaten per day were consumed from tomatoes grown in a home garden without being washed. In addition, we assumed there would be no degradation in the preparation process. Acute ingestion was estimated by

$$PE_{Ingestion} = [(AEC \times CF) \times SAT]/BW \quad (2)$$

where $PE_{Ingestion}$ is potential exposure from consuming exposed produce (mg/kg BW), AEC is the actual environmental concentration of insecticide that settles onto surfaces (μg/$cm^2$), CF is the conversion from μg/$cm^2$ to mg/$m^2$, SAT is the surface area of tomatoes consumed as estimated by Eifert et al. (2006) ($m^2$), and BW is body weight (kg). The average amount plus the standard error of tomatoes consumed per day by adult males and females, youth, children, toddlers, and infants is 0.804, 0.804, 0.874, 1.19, 1.77, and 1.21 g/kg BW, respectively (USEPA 1997).

## RESULTS

Two-way ANOVA showed significant differences in *Cx. tarsalis* and *Cx. pipiens* abundance in the $CO_2$-baited traps before and after the applications ($F = 14.59$; df 1, 16; $P = 0.0015$; and $F = 8.49$; df 1, 13; $P = 0.0121$ respectively). There was no interaction between time and treatment, so a paired *t*-test was used to compare

Table 2. Mean female mosquitoes per trap night and standard deviation before and after the insecticide applications inside (spray zone) and outside (control) of the spray area.[1]

| | Spray zone | | Control | |
|---|---|---|---|---|
| Species, trap type | Before | After | Before | After |
| *Culex pipiens*, $CO_2$ traps | 4.94 (4.70) a | 2.46 (2.24) b | 10.33 (13.59) a | 8.48 (13.68) a |
| *Culex pipiens*, gravid traps | 14.79 (12.27) a | 9.79 (9.75) a | 12.33 (12.50) a | 14.47 (9.65) a |
| *Culex tarsalis*, $CO_2$ traps | 8.75 (7.44) a | 3.00 (1.61) b | 17.78 (19.08) a | 14.28 (20.00) a |

[1] Means within a column in spray zone or control followed by the same letter were not significantly different ($P > 0.05$).

abundance before and after in the spray zone and control areas separately. There was a significant reduction in abundance of host-seeking *Cx. tarsalis* and *Cx. pipiens* inside of the spray zone and not in the untreated control areas (Table 2). There was no significant difference in the number of *Cx. pipiens* females captured by the gravid traps before and after the aerial adulticide applications in the spray zone or in the control areas. Percentage of reduction calculated by Mulla's formula was estimated to be 57.33% for *Cx. tarsalis* and 40.81% for *Cx. pipiens*.

Maximum likelihood estimates of WNV infection rates for *Cx. pipiens* and *Cx. tarsalis* before and after the application events are shown in Table 3. Infection rates for *Cx. tarsalis* decreased significantly in the spray zone after the aerial adulticide applications, but not for *Cx. pipiens*. In contrast, infection rates for both species increased in the untreated control area after the applications. Percentage of reduction of the minimum infection rates calculated by Mulla's formula was estimated to be 77.41% for *Cx. tarsalis* and 21.56% for *Cx. pipiens*.

Sentinel cage bioassay data showed that average mortality 1 h after application was 40% (range 0% to 91%) for *Cx. pipiens* and 51% (range 0% to 94%) for *Cx. tarsalis*. Results for mortality at 1, 2, and 12 h are shown in Table 4. We observed a high variability among sentinel cage mortality, suggesting that the insecticide application did not reach all sites. Nonetheless, mortality of mosquitoes in the sentinel cages in the spray zone was significantly different than mortality at the untreated control area ($F = 142.91$; $P < 0.0001$ and $F = 185.34$; $P < 0.0001$ for *Cx. pipiens* and *Cx. tarsalis*, respectively).

The human health risk assessment from exposure to three aerial ULV applications of pyrethrins and PBO at rates used by the SYMVCD indicated that total acute exposure for pyrethrins at the 95th percentile of exposure ranged from 0.000004 to 0.0003 mg/kg BW/day for the groups assessed (Table 5). Risk quotients for pyrethrins at the 95th percentile ranged from 0.00003 to 0.002 for all groups (Table 6). Total acute exposure for PBO at the 95th percentile ranged from 0.00008 to 0.003 mg/kg BW/day for the groups assessed (Table 5). Risk quotients for PBO at the 95th percentile ranged from 0.00001 to 0.0005 for all groups (Table 6). No chemical or group exceeded the RQ LOC. Toddlers and infants were the highest-risk groups whereas adult males were the lowest-risk group assessed in this study (Table 6).

Our results showed that median inhalation exposure contributed <0.01% to the overall exposure of all groups. Median dermal exposure contributed about 53% to the overall exposure of adult males and females, youth, and children; however, the median dermal exposure only contributed 18% to the overall exposure of toddlers and infants. Median exposure from hand-to-mouth exposure from insecticide settling onto their hand contributed about 17% to the overall exposure of toddlers and infants. Median exposure from hand-to-mouth turf-dislodgeable residue contributed about 16% to the overall

Table 3. Maximum likelihood estimates of WNV infection rates for mosquito pools collected in the spray zone and untreated control area before and after the application events.

| Area | Time | Species | MLE[1] (95% CI) | No. females | No. pools | No. positive pools | % positive pools |
|---|---|---|---|---|---|---|---|
| Spray zone | Before | *Culex pipiens* | 7.87 (5.02–11.86) | 2,968 | 188 | 21 | 11.17 |
| | | *Culex tarsalis* | 10.85 (6.54–17.09) | 1,605 | 118 | 16 | 13.56 |
| | After | *Culex pipiens* | 7.51 (2.82–16.65) | 705 | 69 | 5 | 7.25 |
| | | *Culex tarsalis* | 3.42 (0.20–16.54) | 292 | 50 | 1 | 2.00 |
| Control | Before | *Culex pipiens* | 5.31 (1.76–12.70) | 781 | 45 | 4 | 8.89 |
| | | *Culex tarsalis* | 4.53 (1.51–10.81) | 910 | 37 | 4 | 10.81 |
| | After | *Culex pipiens* | 6.46 (2.84–12.92) | 1,205 | 68 | 7 | 10.29 |
| | | *Culex tarsalis* | 6.32 (2.38–14.05) | 855 | 47 | 5 | 10.64 |

[1] MLE, bias-corrected maximum likelihood estimate of infection rate in 1,000 mosquitoes (Biggerstaff 2006); CI, confidence interval.

Table 4. *Culex pipiens* and *Culex tarsalis* average percentage of mortality (standard deviation) in bioassay cages.

| | Spray zone | | Control | |
|---|---|---|---|---|
| Time (hr) | *Cx. pipiens* | *Cx. tarsalis* | *Cx. pipiens* | *Cx. tarsalis* |
| 1 | 40.07 (25.83)[1] | 51.41 (29.03)[2] | 2.94 (12.13) | 8.51 (23.95) |
| 2 | 56.47 (26.3)[1] | 72.27 (29.43)[2] | 6.96 (18.28) | 9.14 (24.8) |
| 12 | 68.48 (28.48)[1] | 86.56 (21.74)[2] | 7.55 (18.2) | 9.14 (24.8) |

[1] Significantly different than *Cx. pipiens* control ($P < 0.05$).
[2] Significantly different than *Cx. tarsalis* control ($P < 0.05$).

exposure of toddlers and infants. Mean ingestion exposure contributed about 43% to the overall exposure of all groups.

## DISCUSSION

Although evaluation of efficacy is an essential component of assessing pesticide applications (Carney et al. 2008) and vector abundance is an important measure of efficacy of control strategies (Nielsen et al. 2007), it remains a difficult task for mosquito control districts because there are many variables that cannot be controlled. In 2007, when the decision was made to conduct aerial applications of pyrethrins and PBO to manage adult populations of mosquitoes in the north Sacramento area, the District selected areas outside of the aerial spray zone to be the untreated control sites, and as such, they should not have received any insecticide application. But as a vector control agency, once one of these control sites shows either high abundance of mosquitoes or positive mosquito pools, it is the District's responsibility to respond to those surveillance parameters and follow its management plan. Therefore, although the control sites were not sprayed aerially, some did receive ground treatments with trucks and backpack foggers in response to high trap counts, positive dead birds, and positive mosquito pools. Although this may be a confounding factor when comparing abundance of mosquitoes and infection rates inside and outside of the aerial spray zone, our results showed significant differences in abundance between the two areas even in the presence of ground treatments at the control sites. Another variable out of our control is that mosquito abundance tends to vary markedly among trap sites. Moreover, routine vector control strategies continued to be conducted by SYMVCD following its IPM program, and source reduction and larvicide applications were performed before, during, and after the aerial adulticide applications throughout all areas of Sacramento and Yolo counties.

Our analysis indicates that the aerial applications were made at a time when *Cx. pipiens* populations in Sacramento County were already declining, but *Cx. tarsalis* populations were increasing. Analysis of the data and population trends indicate that most *Cx. pipiens* collected at the time of the aerial adulticide applications were gravid females, suggesting that the population of these mosquitoes was composed of older, blood-fed females, presenting a different behavior than the host-seeking mosquitoes. That may explain why there was a greater reduction in host-seeking *Cx. tarsalis* than *Cx. pipiens*. Nonetheless, there was still a significant reduction in host-seeking *Cx. pipiens* abundance in the spray zone. Although not statistically significant, a reduction of 33.8% in *Cx. pipiens* captured in gravid traps was also observed in the spray zone. That is important because, at the same time, *Cx. pipiens* captured in gravid traps in the untreated control area increased 17.4%.

Sentinel mosquitoes were used to evaluate the deposition of the pesticide into the target areas.

Table 5. Acute total potential exposure means at 50th and 95th percentile confidence intervals for each group and chemical assessed.

| Chemical | PE[1] | Adult males[2] | Adult females[3] | Youth[4] | Children[5] | Toddlers[6] | Infants[7] |
|---|---|---|---|---|---|---|---|
| Pyrethrins | 50th | 0.000001 | 0.000001 | 0.000002 | 0.000003 | 0.00001 | 0.00002 |
| | 95th | 0.000005 | 0.000005 | 0.000008 | 0.00001 | 0.00005 | 0.00009 |
| Piperonyl butoxide | 50th | 0.00003 | 0.00003 | 0.00004 | 0.00006 | 0.0001 | 0.0003 |
| | 95th | 0.0001 | 0.0001 | 0.0002 | 0.0002 | 0.0006 | 0.001 |

[1] PE, potential exposure. Total acute exposure to each active ingredient for each group was estimated by adding together inhalation, dermal, hand-to-mouth, turf-dislodgeable, and ingestion exposure routes (mg/kg body weight/day).
[2] 18–65 years of age.
[3] 18–65 years of age.
[4] 10–12 years of age.
[5] 5–6 years of age.
[6] 2–3 years of age.
[7] 0.5–1.5 years of age.

Table 6. Acute risk quotient means at 50th and 95th percentile confidence intervals for each group and chemical assessed.

| Chemical | RQ[1] | Adult males[2] | Adult females[3] | Youth[4] | Children[5] | Toddlers[6] | Infants[7] |
|---|---|---|---|---|---|---|---|
| Pyrethrins | 50th | 0.000008 | 0.00001 | 0.00001 | 0.00002 | 0.00008 | 0.0002 |
| | 95th | 0.00003 | 0.00004 | 0.00006 | 0.0001 | 0.0004 | 0.0007 |
| Piperonyl butoxide | 50th | 0.000004 | 0.000005 | 0.000006 | 0.000009 | 0.00002 | 0.00004 |
| | 95th | 0.00002 | 0.00002 | 0.00003 | 0.00004 | 0.0001 | 0.0002 |

[1] Risk quotient.
[2] 18–65 years of age.
[3] 18–65 years of age.
[4] 10–12 years of age.
[5] 5–6 years of age.
[6] 2–3 years of age.
[7] 0.5–1.5 years of age.

Deposition may be markedly altered by local meteorological conditions that are affected by the presence of heavy vegetation (Barber et al. 2007, Elnaiem et al. 2008), which also filters out the pesticide (Taylor and Schoof 1971). To penetrate the canopy, wind direction must be perpendicular to the spray line and wind speeds must move the pesticide through the canopy (Barber et al. 2007). Wind direction and speed are usually measured at the application point, but may be different from conditions at vegetated locations. Mortality results from our bioassay cages varied significantly, with different locations presenting very low mortality at different application events. Environmental conditions may have been responsible for the reduced spray movement through some of these target zones in different days.

The probabilistic risk assessment showed that RQs for a single truck-mounted application are about 10-fold greater than those estimated for three applications of aerial ULV. Although the rates used for aerial applications may be greater than for truck-mounted, deposition on the ground is lower after aerial ULV (Lothrop et al. 2007, Schleier and Peterson 2009, Schleier et al. 2009b). These results support the findings of previous risk assessments and regulatory documents that the risks from aerial ULV are lower than those of truck-mounted ULV (NYCDOH 2005, Peterson et al. 2006). Our results are supported by biomonitoring studies that showed no increase in urinary metabolites after aerial ULV applications of naled (Kutz and Strassman 1977, Duprey et al. 2008). Our assessment determined that exposures after three aerial ULV applications are 0.001% of the acute RfD, and are below regulatory LOCs.

The main objective of the aerial adulticide applications conducted by SYMVCD in 2007 was to decrease the number of infected and infective adult mosquitoes in the target area. Infection rates were significantly lower for *Cx. tarsalis* in the spray zone after the aerial adulticide applications, but not in the control areas. Even though we did not observe a significant decrease in the maximum likelihood estimate of minimum infection rates for *Cx. pipiens* in the spray zone, rates for this species were also higher in the control areas after the application events, and more positive mosquito pools were found in the control area after the adulticide applications than before. Therefore, our data indicate that the aerial ULV treatments conducted by the SYMVCD in 2007 may have reduced the risk of WNV transmission to humans by effectively reducing the population of infected adult mosquitoes at the target area. The probabilistic risk assessment suggests that human risk from exposure to the insecticide applications was below regulatory levels of concern, so the benefits likely exceeded risks. The current weight of evidence from biomonitoring, epidemiology, risk assessments, and reduction in disease incidence rates after ULV applications (Kutz and Strassman 1977; Karpati et al. 2004; Currier et al. 2005; O'Sullivan et al. 2005; Carr et al. 2006; Peterson et al. 2006; Macedo et al. 2007b; Duprey et al. 2008; Schleier et al. 2009a, 2009b) demonstrate that the benefit of reducing WNV incidence rates outweigh public health risks from insecticide applications to manage adult mosquitoes.

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# Efficacy of Aerial Spraying of Mosquito Adulticide in Reducing Incidence of West Nile Virus, California, 2005

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Epidemic transmission of West Nile virus (WNV) in Sacramento County, California, in 2005 prompted aerial application of pyrethrin, a mosquito adulticide, over a large urban area. Statistical analyses of geographic information system datasets indicated that adulticiding reduced the number of human WNV cases within 2 treated areas compared with the untreated area of the county. When we adjusted for maximum incubation period of the virus from infection to onset of symptoms, no new cases were reported in either of the treated areas after adulticiding; 18 new cases were reported in the untreated area of Sacramento County during this time. Results indicated that the odds of infection after spraying were ≈6× higher in the untreated area than in treated areas, and that the treatments successfully disrupted the WNV transmission cycle. Our results provide direct evidence that aerial mosquito adulticiding is effective in reducing human illness and potential death from WNV infection.

*West Nile virus* (WNV; genus *Flavivirus*, family *Flaviviridae*) is transmitted to humans through the bite of an infected female mosquito and can cause clinical manifestations such as acute febrile illness, encephalitis, flaccid paralysis, and death (*1*). In California, WNV was first identified in 2003, during which time the virus was detected in 6 southern counties and 3 infected persons were identified (*2*). The following year, WNV spread northward from southern California to all 58 counties in the state, resulting in 779 human WNV cases and 28 deaths (*3,4*). In 2005, 880 human WNV cases and 19 related deaths were identified in California; 3,000 cases were reported nationwide (*5,6*). In contrast to 2004, when most of the WNV activity was concentrated in southern California, activity in 2005 occurred primarily in the northern part of the Central Valley of California, where Sacramento County, the epicenter of WNV activity in the United States that year, had more human cases (163) than any other county in the nation (*7*).

In northern California, the principal urban and rural vectors of WNV are *Culex pipiens* and *Cx. tarsalis*, respectively (*8–10*). To reduce WNV transmission and human exposure to mosquitoes in 2005, the Sacramento-Yolo Mosquito and Vector Control District (SYMVCD) implemented a battery of control practices from their Integrated Pest Management plan (*11*), an ecosystem-based strategy focused on long-term control of mosquito populations (D. Brown, SYMVCD, pers. comm.). Despite the district's intensified efforts (which began in March 2005) to control larval mosquitoes and to spot-treat for adult mosquitoes by using truck-mounted equipment, by August 2005 the county had reached the epidemic response level designated by the California Mosquito-Borne Virus Surveillance and Response Plan (*12,13*). Per the response plan, SYMVCD determined the appropriate response and control measures through the analysis of 8 surveillance factors, which provided a semiquantitative measure of transmission risk (D. Brown, pers. comm.). Rapidly escalating risk for WNV transmission to humans in Sacramento County was indicated by high mosquito abundance and infection prevalence; high numbers of sentinel chicken seroconversions;

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and record numbers of dead bird reports, equine cases, and human cases, including ≈24 confirmed human infections by early August (*8,10,14*). Following state guidelines, and in consultation with local public health officials, SYMVCD initiated aerial adulticiding in Sacramento County in August 2005 to rapidly reduce the abundance of infected mosquitoes and decrease the risk for WNV transmission to humans (D. Brown, pers. comm.). Despite a 60-year history of the aerial application of mosquito control products in California (*15*), this was the first instance within the state of aerial adulticiding over a large urban area.

Although published studies on aerial application of adulticides have documented reductions in mosquito abundance and infection prevalence along with concurrent or subsequent decreases in human cases (*16–19*), no published study to date has directly assessed the efficacy of such control efforts in reducing incidence of human disease by comparing distribution of clinical cases within treated and untreated areas. The objective of our study was to evaluate the efficacy of adulticide applications for reducing human cases of WNV; we compared the proportion and incidence of cases in the treated and untreated areas of Sacramento County in 2005 before and after aerial treatments. The proportion and incidence of these cases were also compared with those of the rest of California.

## Methods

### Data Collection

Human WNV case data were reported to the California Department of Public Health from the Sacramento County Department of Health and Human Services and other local health departments throughout the state by using a standardized case history form. A total of 177 human infections were reported within Sacramento County in 2005, with onsets of illness ranging from June through October. Of 177 infections, 163 were clinical cases and 14 were asymptomatic infections; the former was confirmed by immunoglobulin (Ig) G and IgM antibody assays of serum or cerebrospinal fluid samples. Of 163 case records, 7 had no date-of-onset information and 4 others had no residential address. Consequently, the Sacramento County human dataset used in this study comprised 152 records that contained spatial and temporal attributes.

Residential addresses were imported into ArcMap 9.1 geographic information systems software (Environmental Systems Research Institute, Inc., Redlands, CA, USA) and geocoded by using the software's 2005 StreetMap USA Plus AltNames street dataset. All remaining unmatched addresses were geocoded by using Tele Atlas 2006 (Tele Atlas, Lebanon, NH, USA), NAVTEQ 2006 (NAVTEQ, Chicago, IL, USA.), GDT 2005 (Geographic Data Technology, Inc., Lebanon, NH, USA), and TIGER 2006 (US Census Bureau, Washington, DC, USA) datasets. Population size estimates for the study areas defined below were calculated in ArcMap by selecting census blocks that had their center (centroid) in each defined region (Table 1) (*20*). All data were mapped by using the NAD83 USA Contiguous Albers Equal Area Conic coordinate system.

### Adulticide Application

Aerial adulticide applications were intended to create aerosolized clouds of insecticide that would contact, and consequently kill, airborne adult *Culex* spp. mosquitoes. SYMVCD targeted areas for treatment on the basis of levels of mosquito infection prevalence that had been previously associated with epidemic transmission within an urban setting (minimum infection rate per 1,000 female *Culex* spp. tested >5.0) (*12*). The district contracted with ADAPCO Vector Control Services (ADAPCO, Inc., Sanford, FL, USA) to apply adulticide by using 2 Piper Aztec aircraft (Piper Aircraft, Inc., Vero Beach, FL, USA) over an area of 222 km$^2$ in northern Sacramento County on the nights of August 8–10, 2005 (northern treated area) and an area to the south of 255 km$^2$

Table 1. Number of human cases of infection with West Nile virus by location and temporal classification, California, 2005*

| Area† | Total | Pretreatment‡ | Posttreatment§ | Postincubation¶ | Population# |
|---|---|---|---|---|---|
| Treated, northern | 34 | 28 | 6 | 0 | 221,828 |
| Treated, southern | 21 | 20 | 1 | 0 | 338,579 |
| Buffer, northern | 13 | 9 | 4 | 3 | 94,399 |
| Buffer, southern | 8 | 5 | 3 | 1 | 50,127 |
| Untreated | 76 | 41 | 35 | 18 | 518,566 |
| Sacramento County | 152 | 103 | 49 | 22 | 1,223,499 |
| California | 670 | 357 | 313 | 197 | 32,648,149 |

*Only cases with known date of onset of illness and location information (i.e., Sacramento County at the address level and California at the county level) are included in the analysis.
†California excluding Sacramento County.
‡Refers to cases with onset of illness up to and including the last date that aerial adulticiding was conducted (ending 22 Aug for the southern treated area and southern buffer zone and 10 Aug for all other areas).
§Refers to cases with onset of illness after the last date that aerial adulticiding was conducted (beginning 23 Aug for the southern treated area and southern buffer zone and 11 Aug for all other areas).
¶Refers to cases with onset of illness >14 days after the first date that aerial adulticiding was conducted (beginning 4 Sep for the southern treated area and southern buffer zone and 23 Aug for all other areas).
#Population data source: UA Census 2000 TIGER/Line data made available in shapefile format through Environmental Systems Research Institute, Inc. (Redlands, CA, USA) (*20*).

on the nights of August 20–22, 2005 (southern treated area) (D. Brown, unpub. data) (Figure 1). Coverage was similar each night; repeated applications were intended to increase efficacy (D. Brown, pers. comm.).

The applied compound was Evergreen EC 60–6 insecticide (MGK, Minneapolis, MN, USA), a product composed of 6% pyrethrin/60% piperonyl butoxide (*8*). It was applied at the maximum rate according to the label, 0.0025 pounds of pyrethrins per acre (ultra-low volume dispersal), by 2 Micronair AU4000 atomizer nozzles (Micron Sprayers, Ltd, Bromyard, Herefordshire, UK) on each aircraft, with a swath width of 1,300 feet and expected droplet spectrum volume mean diameters of 32.1 and 36.3 microns for the 2 planes (D. Brown and G. Goodman, unpub. data). Conditions during each night of spraying included wind speeds of 4–10 knots/h and temperatures/dew points of 27°C/14°C (northern treatment) and 33°C/12°C (southern treatment) (D. Brown, unpub. data). Planes began flying at ≈8:00 PM each night and flew for 3–6 h at 130 knots/h (D. Brown, unpub. data). The aircraft flew at altitudes of 61.0 m in the northern treated area and 91.4 m (because of obstacles such as tall towers and buildings) in the southern treated area (R. Laffey, SYMVCD, unpub. data, D. Markowski, pers. comm.). The Wingman GX aerial guidance and recording system (ADAPCO, Inc.), coupled with the Aircraft Integrated Meteorological Management System (AIMMS-20; Aventech Research, Inc., Barrie, Ontario, Canada), modeled the effective drift of released compounds on the basis of real-time meteorologic conditions (D. Brown, pers. comm.). Flight and treatment data were imported into ArcMap for mapping and analysis.


Figure 1. Map of northern and southern aerial adulticiding treatment areas in Sacramento County, California, 2005, showing the 2 urban areas treated by the Sacramento-Yolo Mosquito and Vector Control District (SYMVCD). Horizontal bars represent swaths of spray clouds created by individual passes of the aircraft, as defined by the spray drift modeling systems. Gaps within spray clouds were caused by factors such as towers and buildings that altered the flight of the aircraft (G. Goodman, SYMVCD, pers. comm.). These gaps were assumed to have negligible effect in this study; no human cases occurred within any gaps. Gray region surrounding much of the spray zones represents the urbanized area of Sacramento; urbanized area is defined by the US Census Bureau as a densely settled territory that contains ≥50,000 persons (*21*). For display purposes, we used the NAD83 HARN California II State Plane coordinate system (Lambert Conformal Conic projection). Inset shows location of treatment areas in California.

### Case Classification and Analysis

Despite the spray drift modeling systems' high degree of accuracy, variable and incomplete spray application was expected at the edges of the modeled spray cloud (D. Markowski, pers. comm.). Factors contributing to this phenomenon include the intrinsic margin of error of the aircrafts' spray drift modeling systems, the extrinsic margin of error caused by factors not detectable or taken into account by the modeling system (i.e., wind gusts, minor changes in aircraft altitude or speed, and other operational variables), and nonoverlapping spray clouds during different nights of application (D. Markowski, pers. comm.). Through consultation with ADAPCO, Inc., this variable and incomplete application at the perimeter was taken into account by delineating a 0.8-km (0.5-mile) buffer within the outermost range of the modeled spray clouds for each treated area (D. Markowski, pers. comm.). Nonbuffered areas of the spray regions (henceforth referred to as treated areas) were considered the most accurate representation of the actual spray application for this analysis, and any WNV cases that occurred within buffer zones were considered separately from those within treated areas. All human cases from Sacramento County that did not occur within treated areas or buffer zones were assigned to the untreated subset of cases, which served as the comparison (control) group for this study.

Cases were further classified by date of onset of illness into pretreatment and posttreatment groups; temporal classification for the untreated area and the rest of California followed that of the northern treated area (Table 1). Because of the relatively lengthy and variable human WNV incubation period, persons who became infected just before the spray events could have become symptomatic up to 14 days later (*22,23*). To exclude from analysis any infections that may have been acquired just before the spray events, posttreatment cases that had an onset of illness >14 days after spraying (counting from the first night of application) were also included in a postincubation subset.

The null hypothesis, that the proportion of cases in treated and untreated areas was equal to that of the respective population size estimates, was tested for pretreatment and posttreatment groups with the exact binomial test for goodness of fit by using VassarStats (http://faculty.vassar.edu/lowry/VassarStats.html). Second, significance of proportions of human cases before and after spraying within treated and untreated areas was evaluated with the Fisher exact test of independence by using SAS version 9.1.3 (SAS Institute Inc., Cary, NC, USA). The null hypothesis of this test was that there was no significant association between occurrence of adulticiding and temporal classification of cases (i.e., pretreatment or posttreatment). Third, relative risk (RR) and odds ratio (OR) of infection in the untreated area compared with those in treated areas were calculated by using cumulative incidence of WNV in each region before and after spraying (*24*). To evaluate whether buffer zones had any effect on results, all calculations were repeated by using cases from buffer zones and treated areas combined, as well as cases from buffer zones alone.

### Assumptions

As is standard practice in most epidemiologic studies, residential addresses of patients were assumed to be locations of disease transmission; this is also consistent with other WNV studies (*25–31*). The assumption that WNV was transmitted to persons at their place of residence is supported by the fact that WNV mosquito vectors feed primarily from dusk to dawn, and also by findings that persons who spent >2 h outdoors during this time without wearing insect repellant had the highest WNV seroprevalence (*31*).

Because of the random sampling requirement for tests of statistical significance, we must assume that various human populations had an equal likelihood of becoming clinically ill before aerial treatment and that no preexisting factors contributed to a differential in disease experience. Although construction of a multilevel, spatial correlation model is beyond the scope of this study, several important properties of the populations sufficiently support our assumption of homogeneity. Despite the geographic size of the untreated area being ≈6× that of the treated areas combined (2,101 vs. 361 km$^2$, Figure 2), population size estimates of both areas were comparable (518,566 vs. 560,407, Table 1) (*20*). Furthermore, the preponderance of cases in the treated (100%, 55/55), buffer (95%, 20/21), and untreated (87%, 66/76) areas was located within the urbanized area of Sacramento, which constitutes 27% (686 of 2,578 km$^2$) of the total area of the county (Figure 1) (*20*). Additionally, most cases in the untreated area were located either between the northern and southern treated areas or immediately north of the northern treated area, and >94% (143/152) of all cases were located within 4.8 km (3 miles) of treated areas. This staggered configuration of treated and untreated areas, along with the general proximity of cases within 1 urban region, supported the assumption of homogeneity of populations at risk and created a natural experiment for comparative analyses between treated and untreated areas.

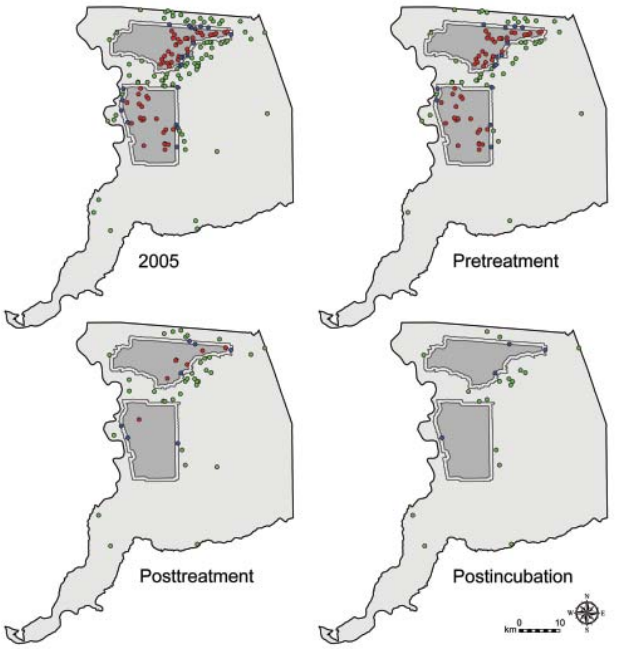


Figure 2. Locations of treated areas and human cases of West Nile virus by temporal classification, Sacramento County, California, 2005. Shown are treated areas (dark gray), surrounding 0.8-km buffers (thin regions around dark gray areas), untreated areas (light gray), and location of human cases within each of these regions (red, blue, and green circles, respectively). For display purposes, we used the NAD83 HARN California II State Plane coordinate system (Lambert Conformal Conic projection).

## Results

The observed proportion of pretreatment cases in treated areas to those in the untreated area was not significantly different from the expected proportion on the basis of population size estimates ($p = 0.7508$, Table 2). Similarly, none of the proportions of pretreatment cases in any combination of treated areas and buffer zones were different from those of the untreated area. However, after adulticiding, all proportions of cases in treated areas were lower than that in the untreated area. Proportions of posttreatment cases in buffer zones were not different from those in the untreated area.

There was a significantly lower proportion of posttreatment cases within combined treated areas compared with that in the untreated area ($p<0.0001$, Table 2). Proportions of posttreatment to pretreatment cases within each of the individual treated areas were also significantly lower than that for the untreated area (northern treated area $p = 0.0053$; southern treated area $p = 0.0003$). After com-

Table 2. Statistical test results for West Nile virus cases, Sacramento County, California, 2005*

| | Goodness of fit† | | Independence‡ |
|---|---|---|---|
| Area | Pretreatment | Posttreatment | Posttreatment vs. pretreatment |
| Treated, both | 0.7508 | **<0.0001** | **<0.0001** |
| Treated, northern | 0.0650 | **0.0391** | **0.0053** |
| Treated, southern | 0.2983 | **<0.0001** | **0.0003** |
| Treated plus buffer, both | 0.6195 | **<0.0001** | **0.0005** |
| Treated plus buffer, northern | 0.1015 | **0.0314** | **0.0069** |
| Treated plus buffer, southern | 0.4568 | **<0.0001** | **0.0029** |
| Buffer, both | 0.5140 | 0.5744 | 0.3309 |
| Buffer, northern | 0.5592 | 0.5065 | 0.3745 |
| Buffer, southern | 0.5990 | 1.0000 | 0.7237 |

*Numbers of cases were combined for multiple areas; geographically corresponding buffer zones were added where noted. Numbers are 2-tailed p values. Statistically significant associations (p<0.05) are in **boldface**.
†Exact binomial goodness-of-fit test for observed proportion of cases in listed area(s) to cases in untreated area compared with the expected proportion based on population size estimates.
‡Fisher exact test of independence for 2 × 2 contingency tables containing numbers of pretreatment and posttreatment cases for listed area(s) and the untreated area.

bining cases from treated areas and buffer zones, proportions of posttreatment versus pretreatment cases were again significantly lower (both treated areas plus buffers p = 0.0005; northern treated area plus buffer p = 0.0069; southern treated area plus buffer p = 0.0029). However, none of the proportions of posttreatment versus pretreatment cases in buffer zones alone compared with those in the untreated area were significantly different (both buffer zones p = 0.3309; northern buffer zone p = 0.3745; southern buffer zone p = 0.7237).

The last human case that occurred in treated areas had an onset of illness 12 days after inception of spraying, within the 14-day maximum range of the human WNV incubation period. Thus, when the incubation period was taken into account, there were no new human WNV cases reported in either treated area after adulticiding (postincubation cases, Table 1, Figure 3). In contrast, 18 new cases were reported from the untreated area during this time; the last case occurred 59 days after inception of spraying. The frequency of these postincubation cases relative to the overall number of cases in the untreated area (24%) was consistent with that for the rest of the state (29%) but inconsistent with that for treated areas (0%).

Normalizing number of cases in each region by respective population size estimate showed the increase in incidence levels throughout the year (Figure 4). Statewide (excluding Sacramento County and cases without onset data), cumulative incidence in 2005 was 2.1/100,000 population, and the temporal pattern of incidence throughout the year was similar to that of the untreated area. On the basis of cumulative incidence within each region before aerial treatment, RR for the untreated area compared with that for treated areas was 0.9231 (95% confidence interval [CI] 0.6085–1.400), which did not differ from unity. After treatment, RR was 5.403 (95% CI 2.400–12.16), with an OR of 5.853 (5.403/0.9231, 95% CI 2.351–14.58) in favor of infection in the untreated area than in treated areas; RR and OR differed from unity. Similarly, RRs for the untreated area compared with those for treated areas and buffer zones combined were 0.8990 (95% CI 0.6059–1.334) and 3.398 (95% CI 1.829–6.316) before and after adulticiding, respectively, with an OR of 3.780 (3.398/0.8990, 95% CI 1.813–7.882). Conversely, RRs for the untreated area versus the buffer zones alone were 0.8162 (95% CI 0.4450–1.497) and 1.393 (95% CI 0.6190–3.137) before and after adulticiding, respectively, with an OR of 1.707 (1.393/0.8162, 95% CI 0.6198–4.703); the RRs and OR did not differ from unity.

## Discussion

Evaluation of efficacy is essential for assessing appropriateness of insecticide applications. However, such studies assessing the ability of adulticides to directly affect human incidence of WNV have been nonexistent. Our findings, coupled with corroborating evidence of a reduction in the abundance of *Cx. pipiens* (*8*), indicate that aerial application of pyrethrin in 2005 successfully disrupted the WNV transmission cycle, and that this treatment was responsible for an abrupt decrease in the number of human cases within treated areas compared with that in the untreated area. These results provide direct evidence that aerial spraying to control adult mosquitoes effectively reduced human illness and potential deaths from WNV infection.

With respect to population size estimates, proportions of pretreatment cases in all treated areas and buffer zones were not different from that in the untreated area, which validates comparability of the baseline populations. Similarly, none of the pretreatment RRs deviated from unity, which supports the assumption that treated and untreated areas had an equal likelihood, on the basis of population size, of containing a clinical case before the adulticiding, and that no preexisting factors contributed to differing disease incidence rates during that time. These conditions are important for verifying that the untreated area was a valid

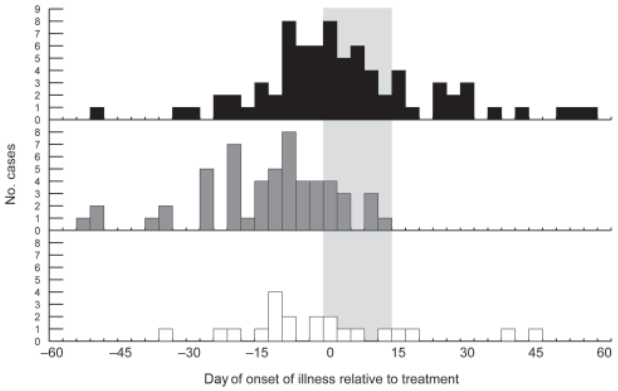


Figure 3. Human cases of West Nile virus (WNV), Sacramento County, California, 2005, by region and date of onset of illness. Black bars show cases within untreated area; gray bars show cases within northern and southern treated areas combined; and white bars show cases within northern and southern buffer zones combined. Values along the x-axis (days) are grouped into sets of 3 and labeled with the date farthest from 0. Each of the 3 days of adulticiding within the treated areas and buffer zones was considered to be 0; for the untreated area, the dates of the northern adulticiding (August 8–10) were considered to be 0. The wide gray vertical band represents time from the first day of treatment to the maximum range of the human WNV incubation period 14 days later.

comparison group for use in statistical analyses.

Comparisons of buffer zones with the untreated area indicated no differences between posttreatment RR or the proportions of posttreatment cases within the 2 areas, which supports the assumption of reduced spray efficacy at the perimeter of the modeled spray cloud. This finding may have implications for future aerial applications and efficacy studies. Additionally, posttreatment infiltration of *Cx. tarsalis* mosquitoes from bordering untreated areas has been a previously documented phenomenon in California and Texas (*19,32–34*). On the basis of mean dispersal distances of *Cx. tarsalis* (0.88 km) and *Cx. pipiens quinquefasciatus* (1.10 km) in California (*35*), use of the 0.8-km buffer in this study also reduced the probability of including in the treatment groups any human infections contracted through posttreatment mosquito infiltration. However, results of all statistical tests remained unchanged after combining the number of cases from buffer zones and treated areas, and these posttreatment reductions of cases still differed from that in the untreated area (Table 2).

Because posttreatment proportions of cases were lower than in the untreated area, we rejected the null hypothesis of goodness-of-fit comparisons. Our results also indicate that there were associations between adulticiding and temporal classification of cases. Therefore, we also rejected the null hypothesis of tests of independence. Furthermore, odds of infection after spraying were ≈6× higher in the untreated area than in treated areas. Without applications of aerial adulticide, more Sacramento residents would have been infected with WNV. This finding supports federal and California WNV response recommendations, which state that "mosquito adulticiding may be the only practical control technique available in situations where surveillance data indicate that it is necessary to reduce the density of adult mosquito populations quickly to lower the risk of WNV transmission to humans" (*36*).

Although there was a negative correlation between aerial treatments and incidence of human cases, causation is predicated upon spraying having a direct effect on mosquito populations. Recent work showed that adulticiding immediately reduced abundance and infection rates of *Culex* spp. mosquitoes compared with rates in an untreated area (*8*). Using factorial 2-way analysis of variance, these researchers compared mean abundances of *Cx. pipiens* and *Cx. tarsalis* from $CO_2$-baited traps (46 trap nights) in the northern treated area with mean abundances from traps (55 trap nights) in similar urban-suburban habitats within the untreated area of Sacramento County and adjacent Yolo County, 1 week before and 1 week after the August 8 spraying. Abundance of *Cx. pipiens* decreased by 75.0%, and there was a significant interaction between adulticiding and temporal classification ($F$ 4.965, df 1,47, p = 0.031).

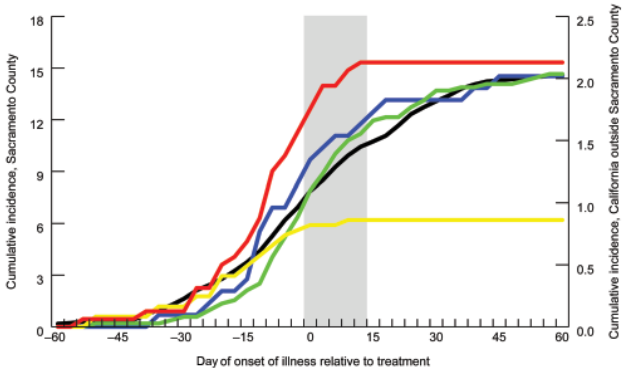


Figure 4. Cumulative incidence of human cases of West Nile virus (WNV) in Sacramento County and California, 2005. Only cases with known date of onset of illness and location information (i.e., Sacramento County at the address level and California at the county level) are included in the analysis. Cumulative incidence is the total no. WNV cases/100,000 population. Green line shows incidence within untreated area; red line shows incidence within northern treated area; yellow line shows incidence within southern treated area; blue line shows incidence within northern and southern buffer zones combined; black line shows incidence within California, excluding Sacramento County. Values along the x-axis (days) are grouped into sets of 3 and labeled with the date farthest from 0. Each of the 3 days of adulticiding within the treated areas and buffer zones was considered to be 0; for the untreated area and the rest of California, the dates of the northern adulticiding (August 8–10) were considered to be 0. The wide gray vertical band represents time from the first day of treatment to the maximum range of the human WNV incubation period 14 days later.

Abundance of *Cx. tarsalis* decreased by 48.7% but the interaction was not statistically significant ($F$ 0.754, df 1,47, p = 0.390). As stated by these researchers, this disparity may have been caused by the presence of "an increasing population of *Cx. pipiens* and an already declining population of *Cx. tarsalis*" at the time of the spraying, and because *Cx. tarsalis* breeds principally in rural areas. Regardless, we reason that *Cx. pipiens* was the primary vector in the Sacramento County epidemic because this species is the principal urban vector in this region (*8–10*), was the most abundant species collected in Sacramento County in 2005 (D.-E.A. Elnaiem, unpub. data), and comprised the highest percentage of WNV-infected mosquito pools (68.3% versus 28.8% for *Cx. tarsalis*) in Sacramento County that same year (*10*).

Additionally, these researchers combined mosquitoes of both species (into pools of ≤50 females) taken from aforementioned traps and others in the northern treated area and untreated area 2 weeks before and 2 weeks after the August 8 adulticiding. Pools of mosquitoes were tested for WNV by using a reverse transcription–polymerase chain reaction, and infection rates were calculated by using a bias-corrected maximum likelihood estimation (www.cdc.gov/ncidod/dvbid/westnile/software.htm). After spraying, infection rates decreased from 8.2 (95% CI 3.1–18.0) to 4.3 (95% CI 0.3–20.3) per 1,000 females in the spray area and increased from 2.0 (95% CI 0.1–9.7) to 8.7 (95% CI 3.3–18.9) per 1,000 females in the untreated area. Furthermore, no additional positive pools were detected in the northern treatment area during the remainder of the year, whereas positive pools were detected in the untreated area until the end of September (D.-E.A. Elnaiem, unpub. data). These independent lines of evidence corroborate our conclusion that actions taken by SYMVCD were effective in disrupting the WNV transmission cycle and reducing human illness and potential deaths associated with WNV.

Historically, human WNV cases in the United States peak in August (*37,38*). This pattern was observed in Sacramento County and the rest of California in 2005, in which 61% (93/152) and 47% (314/670), respectively, of human cases had onset of illness in August. The next highest month was July, during which 27% (41/152) and 29% (195/670) of human cases had onset of illness in the county and the rest of the state, respectively. These findings are consistent with others from Sacramento County in 2005, which indicated that mosquito infection rates peaked in July and August (*10*). Considering early summer amplification within vector populations and length of the human incubation period, WNV remediation efforts would be more effective in limiting illness and death associated with human infection if conducted at the onset of enzootic amplification rather than after occurrence of human cases.

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# Community Aerial Mosquito Control and Naled Exposure

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# COMMUNITY AERIAL MOSQUITO CONTROL AND NALED EXPOSURE

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ABSTRACT. In October 2004, the Florida Department of Health (FLDOH) and the Centers for Disease Control and Prevention (CDC) assessed human exposure to ultra-low volume (ULV) aerial application of naled. Teams administered activity questionnaires regarding pesticide exposure and obtained baseline urine samples to quantify prespray naled metabolite levels. Following the spray event, participants were asked to collect postspray urine specimens within 12 h of the spray event and at 8-h intervals for up to 40 h. Upon completion, a postspray activity questionnaire was administered to study participants. Two hundred five (87%) participants completed the study. The urine analysis showed that although 67% of prespray urine samples had detectable levels of a naled metabolite, the majority of postspray samples were below the limit of detection (<LOD). Only at the "postspray 6" time period, which corresponds to a time greater than 5 half-lives (>40 h) following exposure, the number of samples with detectable levels exceeded 50%. There was a significant decrease in naled metabolites from prespray to postspray (=.02), perhaps associated with a significant reduction (≤0.05) in some participants that may have resulted in pesticide exposure by means other than the mosquito control operations. These data suggest that aerial spraying of naled does not result in increased levels of naled in humans, provided the naled is used according to label instructions.

**KEY WORDS** Mosquito control, naled, exposure assessment, pesticide, ULV application

## INTRODUCTION

Hurricanes and tropical storms often have a significant impact on mosquito-borne diseases because of an increase in mosquito breeding habitats from flooding. In 2004, Florida experienced an extraordinary hurricane season with 4 major hurricanes traversing the state within 3 months. Because of the potential increase in arboviral disease, including West Nile virus (WNV) and eastern equine encephalitis, ultra-low volume (ULV) aerial spraying with the organophosphorus pesticide naled (Dibrom®) was initiated for the control of mosquitoes in areas with known arboviral activity. Although naled has been associated with adverse human health effects after ULV aerial spraying (CDC 2003a), the extent to which humans are exposed to naled during large-scale aerial mosquito control activities has yet to be accurately quantified.

In large-scale mosquito control programs, naled is typically applied via aircraft-mounted sprayers with the inert carrier, naphtha. The ULV pesticide applications use small quantities of active ingredient in relation to the size of the area treated. For effective mosquito control, the maximum rate for ULV surface and aerial application typically is ≤3 oz (85 ml) active ingredient (AI)/acre. These ULV applications aerosolize into very fine droplets that stay aloft and kill mosquitoes on contact. ULV pesticide application is utilized to minimize exposure and risks to people, wildlife, and the environment (U.S. Environmental Protection Agency [EPA] 2002).

Naled is practically nonpersistent in the environment. It rapidly degrades in the presence of sunlight to dichlorvos (Kidd and James 1991). Dichlorvos degrades rapidly with a half-life of less than 8 h in soil and less than 25 h in water (U.S. EPA 1998).

In humans, naled and dichlorvos are rapidly absorbed through the skin and mucous membranes of the digestive and respiratory system and are delivered through the circulatory system to various body tissues. This pesticide is metabolized to a nonspecific organophosphate metabolite, dimethylphosphate (DMP), which is eliminated in the urine within a few days of exposure (National Institutes of Health 2004). Acute

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toxicity of naled is low based on $LC_{50}$ values for dermal, oral, and inhalation exposures in animal studies.

Exposure in humans who remained outside during aerial spraying with a naled and temephos mixture for mosquito control demonstrated urinary DMP increase from a maximum of 60 μg/liter to a maximum of 500 μg/liter within 3 h after spraying (Kutz and Strassman 1977). In a CDC study that involved background levels of 148 environmental chemicals in 2518 urine samples, the median (50th percentile) level for DMP was less than the limit of detection (0.5 μg/liter). The 95th percentile (95% confidence interval) was reported as 13.4 μg/liter (10.9 μg/liter–15.6 μg/liter) (CDC 2003b).

Results from previous studies in Virginia and North Carolina (CDC 2005) suggest that large-scale aerial spraying with naled during mosquito-control activities does not result in significant exposure to pesticides for human populations; however, these studies had statistical limitations. In October 2004, the Florida Department of Health (FLDOH) invited the CDC's National Center for Environmental Health (NCEH) to assess exposure of humans to ULV aerial application of naled in a posthurricane flooded area of Florida. The objectives of this study were to quantify human exposure to naled applied as a ULV aerial pesticide and to overcome statistical limitations of previous similar studies, by increasing the sample size and using participants as their own controls.

## MATERIALS AND METHODS

This study was conducted in St. Johns County, FL, October 2–7, 2004. We employed a prospective cohort study design, and planned to recruit 208 households based on a sample size calculation for adequate statistical power (80%) at the significance level of 0.05. We increased this number to 240 to account for an anticipated attrition rate of 10–15%. Households were chosen from each of the 5 proposed spray zones within St. John's County based on cluster sampling, utilizing census blocks. Thirty-two census blocks (and 5 replacements) were randomly chosen; 7–8 households were surveyed in each of the census blocks. Environmental testing was not part of this study because of the short environmental half-life of naled.

Twelve teams of CDC and FLDOH personnel recruited study participants by going door-to-door within each of the randomly selected census blocks. These teams obtained informed consent from the head of household (or proxy for the head of household), administered questionnaires about household and occupational exposure to pesticides, and obtained a baseline spot urine sample to quantify the concentration of naled metabolites prior to the pesticide spraying. Because DMP is a nonspecific marker of organophosphate exposure, we collected questionnaire data to determine participants' exposure to other pesticides from household or occupational use.

On the evening of October 4, we contacted each participant to inform them of the time of the spray and to ask them to collect postexposure urine specimens on the following day, within 12 h of the spray, and at 8-h intervals for up to 40 h following the spray event. We asked study participants to refrigerate their urine specimens until our teams returned to collect their submissions.

Participants were also asked to note the exact date and time of the urine sample collection. Collection cups were prescreened for pesticides and their degradation products before use in this investigation by CDC laboratories. Once entered into the database, each urine sample was coded into 6 time segment groups of approximately 8-h blocks.

On October 6, teams returned to participant households to collect urine submissions from all study participants and to administer a postspray questionnaire that inquired about their activities during the time since the spraying took place, including any household or occupational exposures to pesticides and any health effects experienced since the spray occurred. Pre- and postspray activities were compared with the use of SAS 9.0, McNemar's test (SAS Institute Inc., Cary, NC), to analyze data from matched pairs of subjects with dichotomous responses. The association between naled metabolite levels and activities was assessed with the use of a Wilcoxon rank sum test. Logistic regression was used to compare the number of increases in naled metabolite levels with the number of decreases; subjects with no change were eliminated from the analysis.

By October 7, all of the urine specimens were sent to the CDC laboratory where they were analyzed for the naled metabolite DMP with the use of gas-tandem mass spectrometry with isotope-dilution quantification. This method can detect differences in the concentration of metabolites at very low levels (micrograms/liter or parts per billion). The use of stable isotope analogues of the metabolites measured also allowed for sample-specific recovery adjustments, producing highly precise results (Bravo et al. 2004). The limit of detection using this method for DMP is 0.5 μg/liter.

## RESULTS

We approached 626 St. John's County residents about volunteering for the study; 235 (43%) agreed to participate. Of these, 205 (87%) participants completed all parts of the study.

Table 1. Ethnicity of St. John's County census versus study participants.

| Ethnicity | 2000 census of St. John's County | 2004 St. John's study |
|---|---|---|
| White | 90.92% | 88.3% |
| African American | 6.29% | 6.8% |
| Hispanic/Latino | 2.6% | 3.4% |
| Native American | 0.26% | 1.0% |
| Asian | 0.95% | 0.5% |
| Pacific Islander | 0.05% | 0.0% |

The mean age of participants was 50.2 years (range 18–76); 44.9% were male. Table 1 compares the ethnicity of the St. John's County census (U.S. Census 2000) with that of our study participants.

Results of the laboratory analysis of urine samples for DMP show that 67% of prespray urine samples had detectable levels of DMP, whereas the majority of postspray samples were below the limit of detection (<LOD) (Table 2). Only at the "postspray 6" time period, which corresponds to a time greater than 5 half-lives following exposure, does the number of samples with detectable levels again exceed 50%. Therefore, the median for the other time periods is less than the limit of detection. Individual changes in urine metabolite levels from pre- to postspray showed a significant decrease in DMP from prespray to postspray samples ($P = 0.02$); 61 individuals showed decreased levels, whereas 38 individuals showed an increase in levels.

Some participants engaged in activities that could potentially lead to other pesticide exposures producing DMP as a metabolite during the time of our study (Table 3). Some activities were reported more often by participants before the spraying occurred than after. For example, more participants handled pesticides, did lawn work, and applied flea products to their pets prior to spraying than after it occurred ($P \leq 0.05$).

Prior to spraying, the most commonly reported activity that could potentially increase urinary pesticide levels was eating fresh produce, with 148 (72.2%) participants reporting that they ate fruits and/or vegetables within 3 days prior to the spray event (51 reported eating no fruits and/or vegetables, 1 was unknown, and 5 values were missing). The 148 participants who reported eating fresh produce prior to spraying had higher median baseline levels of DMP (3.56 μg/liter) than the 51 participants who did not (1.83 μg/liter, $P = 0.03$). Other reported activities were not associated, or only weakly associated, with baseline DMP values.

During our study, several participants reported experiencing nonspecific health-related symptoms. In general, more symptoms were reported by participants prior to the spray event (Table 4) than following it; however, differences are small, except possibly for headaches (Odds ratio = 1.5, $P = 0.07$).

## DISCUSSION

Our study findings suggest that aerial application of naled for large-scale mosquito control did not contribute to urinary DMP levels in the study population. This is consistent with previous findings of studies conducted in North Carolina and Virginia (CDC 2005). Another important finding is that the number of study participants with self-reported symptoms consistent with pesticide poisoning was as large or larger before rather than after the aerial pesticide application. This is consistent with the finding that the acute human-health risks from residential exposure to mosquito insecticides are not expected to exceed levels of concern when they are applied according to labeling guidelines (Peterson et al. 2005).

The findings in this report are subject to several limitations. First, we did not conduct environmental sampling to confirm the presence of the pesticide in or around the homes of study participants. Instead, we obtained projected spray areas from DACS prior to choosing the census tracts in which the study participants were selected. Furthermore, the GIS tracking system on the airplane verified that the study participants were in the spray zone. Our use of self-

Table 2. Sample size, percent detects, and median DMP (dimethyl phosphate) values by sample time period.

| Time period[1] | Number of samples collected | Percent with detectable levels of DMP | Median level of DMP (μg/liter) |
|---|---|---|---|
| Baseline (prespray) | 229 | 67.25 | 3.14 |
| Postspray 1 | 123 | 47.97 | <LOD |
| Postspray 2 | 218 | 40.83 | <LOD |
| Postspray 3 | 223 | 41.70 | <LOD |
| Postspray 4 | 112 | 41.07 | <LOD |
| Postspray 5 | 149 | 32.89 | <LOD |
| Postspray 6 | 28 | 57.14 | 1.85 |

[1] Posttime values as follows: Postspray 1: midnight–0759 h on October 5, 2004, postspray 2: 0800–1559 h on October 5, 2004, postspray 3: 1600–2359 h on October 5, 2004, postspray 4: midnight–0759 h October 6, 2004, postspray 5: 0800–1559 h on October 6, 2004, postspray 6: all later values.

Table 3. Activities associated with potential pesticides exposures, pre- and postspraying.

| Activities (number of total responses) | Total persons engaged in activity, prespray *n* (%) | Total persons engaged in activity, postspray *n* (%) | Subset engaged in activity, pre- and postspray *n* (%) | *P* value[1] |
|---|---|---|---|---|
| Handling pesticides ($n = 203$) | 37 (18.2) | 17 (8.4) | 6 (3.0) | 0.003 |
| Doing field/farm work ($n = 203$) | 7 (3.5) | 4 (2.0) | 3 (1.5) | 0.38 |
| Working in produce stand ($n = 202$) | 1 (0.5) | 1 (0.5) | 0 (0) | 1.00 |
| Doing lawn work ($n = 203$) | 72 (35.5) | 40 (19.7) | 27 (13.3) | <0.01 |
| Applying flea products to pets ($n = 202$) | 16 (7.9) | 7 (3.5) | 3 (1.5) | 0.05 |
| Eating fresh produce ($n = 185$) | 136 (73.5) | 133 (71.9) | 116 (62.7) | 0.74 |

[1] From SAS 9.0, McNemar's test (SAS Institute Inc., Cary, NC).

reported questionnaire data on potential pesticide exposures limits the ability to quantify actual home or occupational pesticide exposure and may have resulted in reduced background exposure during postspray by encouraging residents to avoid these activities that they just learned resulted in pesticide exposure. The lack of increase in DMP urine levels following aerial spraying could be because study participants were told when the spraying was going to occur and these participants could have modified their activities (i.e., stayed indoors, turned air conditioning to recirculate, etc.) to avoid exposure.

Some participants had measurable levels of DMP prior to spraying, which suggests that participants had been exposed to pesticides or their environmental degradation products at home or at work (Grey et al. 2005). A study by Lewis et al. (1994) demonstrated exposure to pesticides in the home through household dust and soil exposure containing pesticides. Schools, playgrounds, day-care, and commercial business settings, especially with recent pesticide application, also represent potential exposure sites (Krieger et al. 2001; Alarcon et al. 2005). Dietary intake, such as eating fresh fruits and vegetables, can also be a significant pathway of environmental exposure to pesticides (Pang et al. 2002). The studies' findings of increased baseline levels of DMP in persons who reported eating fresh produce (3.56 μg/liter) to persons who did not report consumption of fresh produce (1.83 μg/liter) were comparable to findings published in CDC, 2005 (3.2 μg/liter and 1.4 μg/liter, respectively).

Although toxicity of mosquito-control adulticides is relatively low, the public perception of the health risks associated with mosquito control is quite high (Roche 2002). Although monitoring potential human exposure to pesticides from aerial spraying is important for communities with large-scale mosquito-control efforts, our study suggests that emergency aerial spraying with ULV naled was not associated with an increase in urine pesticide metabolite concentrations in residents within the spray area when these residents were provided advance notification of the aerial pesticide application.

The Florida Pesticide Surveillance Program (PESP) received 2 reports of people living within the study area who experienced symptoms possibly related to exposure to mosquito control activities during the time of our study. In the first report, a 14-yr-old male experienced burning of the skin and eye irritation moments after the aerial spraying event and reported direct contact with droplets. The second report detailed a female aged 7 years with a history of asthma who experienced a rash, breathing problems, and chest pain while waiting for the bus the morning after the spray event. The symptoms reported by the 14-year-old were mild and resolved without any medical intervention. The 7-year-old female required medical treatment, after which her symptoms resolved. Both cases were classified as possible pesticide poisonings with the use of the CDC/NIOSH (National Institute of Occupational Safety and Health) classification (Krieger et al. 2001). Neither of these people were subjects in our study and we did not have urinary DMP

Table 4. Reported symptoms associated with potential pesticide exposure, pre- and post spraying.

| Symptom (number of total responses) | Total persons reporting symptom, prespray *n* (%) | Total persons reporting symptom, postspray *n* (%) | Subset reporting symptoms pre- and postspray *N* (%) | *P* value[1] |
|---|---|---|---|---|
| Nausea ($n = 196$) | 10 (5.1) | 10 (5.1) | 4 (2.0) | 1.0 |
| Vomiting ($n = 197$) | 3 (1.5) | 2 (1.0) | 1 (0.5) | 1.0 |
| Diarrhea ($n = 196$) | 3 (1.5) | 4 (2.0) | 1 (0.5) | 1.0 |
| Abdominal cramps ($n = 196$) | 10 (5.1) | 9 (4.6) | 5 (2.6) | 1.0 |
| Headache ($n = 199$) | 37 (18.6) | 26 (13.0) | 16 (8.0) | 0.07 |
| Trembling ($n = 197$) | 6 (3.0) | 3 (1.5) | 3 (1.5) | 0.25 |

[1] from McNemar's test.

levels on either of them. No other cases were reported.

These possible pesticide exposures highlight the importance of alerting populations living in areas where ULV pesticides will be applied of the planned spray event so they make take actions to limit their exposure. This is particularly important for vulnerable populations, such as young children or people with established sensitivity, as they may be more susceptible to adverse reactions from exposure than healthy adults.

The ULV applications of mosquito control pesticides, both aerial and truck mounted, are an important tool in the public health response to arboviruses. Future studies are needed to address the long-term safety of low-concentration chronic exposure to naled and other mosquito control pesticides such as pyrethrins and pyrethroids. In addition, public health interventions that reduce home and workplace exposure to pesticides may be needed.

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# Impact of Aerial Spraying of Pyrethrin Insecticide on *Culex pipiens* and *Culex tarsalis* (Diptera: Culicidae) Abundance and West Nile Virus Infection Rates in an Urban/Suburban Area of Sacramento County, California

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**ABSTRACT** In response to an epidemic amplification of West Nile virus (family *Flaviviridae*, genus *Flavivirus*, WNV), the Sacramento and Yolo Mosquito and Vector Control District (SYMVCD) sprayed ultralow-volume (ULV) formulations of pyrethrin insecticide (Evergreen EC 60-6: 6% pyrethrin insecticide, 60% piperonyl butoxide; MGK, Minneapolis, MN, applied as 0.003 kg/ha [0.0025 lb/acre]) over 218 $km^2$ in north Sacramento and 243.5 $km^2$ in south Sacramento on three consecutive evenings in August 2005. We evaluated the impact of this intervention in north Sacramento on the abundance and WNV infection rates of *Culex pipiens* L. and *Culex tarsalis* Coquillett. Mortality rates of caged *Cx. tarsalis* sentinels ranged from 0% under dense canopy to 100% in open fields. A comparison of weekly geometric mean mosquito abundance in $CO_2$-baited traps in sprayed and unsprayed areas before and after treatment indicated a 75.0 and 48.7% reduction in the abundance of *Cx. pipiens* and *Cx. tarsalis*, respectively. This reduction was statistically significant for *Cx. pipiens*, the primary vector of WNV, with highest abundance in this urban area, but not for *Cx. tarsalis*, which is more associated with rural areas. The infection rates of WNV in *Cx. pipiens* and *Cx. tarsalis* collected from the spray zone were 8.2 and 4.3 per 1,000 female mosquitoes in the 2 wk before and the 2 wk after applications of insecticide, respectively. In comparison, WNV infection rates in *Cx. pipiens* and *Cx. tarsalis* collected at same time interval in the unsprayed zone were 2.0 and 8.7 per 1,000, respectively. Based on the reduction in vector abundance and its effects on number of infective bites received by human population, we concluded that the aerial application of pyrethrin insecticide reduced the transmission intensity of WNV and decreased the risk of human infection.

**KEY WORDS** West Nile virus, vector-borne disease, mosquitoes, California, control

The intensity of West Nile virus (family *Flaviviridae*, genus *Flavivirus*, WNV) transmission to humans is dependent upon the level of enzootic amplification, which, in turn, is related to mosquito abundance, infection rates, and feeding patterns as well as local ecology and behavior that influence human exposure (Komar 2000, Hayes 2005). In California, practically all mosquito species found naturally infected with WNV are within the genus *Culex*, with *Culex pipiens* L. and *Culex tarsalis* Coquillett infected most frequently in the Sacramento Valley (Hom et al. 2005, Hom et al. 2006). Other California species have been found to be competent laboratory vectors (Goddard et al. 2002), but they rarely are infected in nature; therefore, they are presumed to be of minimal epidemiological importance. Based on previously published host selection studies (Tempelis et al. 1965, Tempelis and Washino 1967), *Cx. pipiens* and *Cx. tarsalis* likely function as maintenance, amplifying, and bridge vectors.

WNV first was detected in California during 2003, but it was restricted to areas south of the Tehachapi Mountains (Reisen et al. 2004). The next year, WNV amplified to epidemic levels in southern California and spread northward to all 58 counties, including Sacramento County where it was associated with low-level transmission to humans and horses (Hom et al. 2005; Armijos et al. 2005). Subsequently in 2005, a severe WNV outbreak occurred in Sacramento County, with 177 human infection cases (incidence of 14.5 cases per 100,000), 40 equine cases, 16,900 reported dead birds, and a 53% seroconversion rate in

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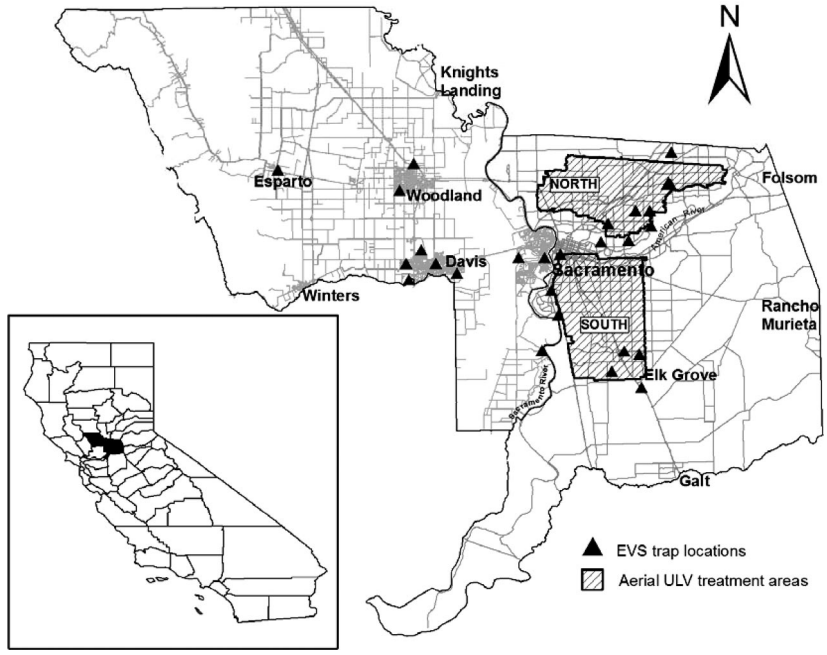


**Fig. 1.** Map of Sacramento and Yolo counties, CA, showing location of mosquito trapping sites (▲) and area subjected to aerial spraying of pyrethrin insecticide in north Sacramento (north) and south Sacramento (south). Inset, location in California.

110 sentinel chickens (Elnaiem et al. 2006). During this outbreak, WNV infection was detected in 139 of 1,896 pools (7.3%) containing 34,386 female mosquitoes. *Cx. pipiens* and *Cx. tarsalis* made up 68.3 and 28.8% of the infected pools, respectively. Other mosquito species found infected were *Culex erythrothorax* Dyar (0.7% of the infected pools), *Culex thriambus* Dyar (0.7% of the infected pools), and *Culex stigmatosoma* Dyar (1.4% of the infected pools) (Elnaiem et al. 2006).

During the early phase of the 2005 outbreak, the Sacramento and Yolo Mosquito and Vector Control District (SYMVCD) used intensive larviciding and public education to suppress vector abundance and limit human exposure, respectively. In response to very high focal mosquito infection rates, the clustering of dead American crows (AMCR), and an elevated risk for human infection, and following the guidelines of California Mosquito-Borne Virus Surveillance and Response Plan (Barker et al. 2003; Kramer 2005), SYMVCD intervened by applying adulticides. Mosquito adult control initially was attempted with 5% pyrethrin/25% piperonyl butoxide (PBO) applied by ground ultralow-volume (ULV) equipment at scattered sites in Sacramento and Yolo counties. As it became clear that epidemic transmission of WNV was occurring over large urban–suburban areas in north (218.5 $km^2$) and south Sacramento (243.5 $km^2$), SYMVCD contracted two aircraft to spray ULV formulations of the pyrethrin insecticide Evergreen over these two areas on 8–10 and 20–22 August 2005, respectively. Although these applications initiated debate over the effectiveness and the environmental and health risks of aerial spraying of insecticides against WNV transmission in an urban setting (Weston et al. 2006), these spray events effectively interrupted epidemic transmission (Carney et al. 2008). In the current article, we describe the impact of aerial spraying of pyrethrin insecticide on *Cx. tarsalis* and *Cx. pipiens* abundance and infection rates with WNV in north Sacramento Spray zone. The evaluation study was limited to the north Sacramento Spray zone, because of lack of adequate mosquito trapping data in the south Sacramento Spray zone.

## Materials and Methods

**Study Area.** Located in the middle of the Central Valley of California, Sacramento County covers 2,578 $km^2$ and supports a human population of 1,223,499 (Fig. 1). The climate is Mediterranean, characterized by a mild wet winter and hot dry summer. In 2005, this area experienced above-average summer temperatures, reaching daily averages of 26.4 and 24.9°C for July and August, respectively. During the 2 wk before and after the application of insecticide in north Sacramento spray area, the daily minimum-maximum temperatures were 17–37°C, 16–38°C, 16–36°C, and 14–31°C, respectively (Sacramento International Airport weather station).

**Aerial Spraying.** SYMVCD contracted with ADAPCO Vector Control Services (ADAPCO, Inc., Sanford, FL), which used two Piper Aztec aircraft (flight speed 130 knots, elevation 61 m [200 feet]) to apply Evergreen Crop Protection EC 60-6 (6% pyrethrin insecticide, 60% PBO, MGK, Minneapolis, MN),

over a 218.5-km$^2$ area in north Sacramento and a 243.5-km$^2$ area in south Sacramento (Fig. 1). Using AU 4000 Micronair nozzles (Micron Sprayers Ltd., Bromyard Industrial Estate, Bromyard, Herefordshire, United Kingdom), the insecticide was applied at 0.003 kg/ha (0.0025 lb/acre), the maximum rate permitted by the label. The spraying in north Sacramento was conducted on three consecutive nights during 8–10 August 2005. Ground level wind speed ranged from 4 to 10 knots, temperature averaged 27°C, and the dew point was 24°C. The application in south Sacramento was conducted during 20–22 August 2005.

**Mosquito Abundance and Infection with WNV.** Efficacy of insecticide spraying was measured by mortality of sentinel *Cx. tarsalis* from a laboratory colony with known susceptibility for pyrethrins. Mosquitoes were exposed from 20 to 2400 hours within sentinel cages (Townzen and Natvig 1973) placed at replicate sites representing an open field, an apartment complex and a creek (Brook Tree Park and Coyle Creek). Cages were removed 30 min after the completion of spray, examined for immediate mosquito mortality, placed in plastic bags, transported to the SYMVCD laboratory, held for 12 h, and then examined for mortality. Results were expressed as percentage of mortality for each cage of 12–28 mosquitoes.

Mosquito abundance was measured by $CO_2$-baited traps (Rohe and Fall 1979), placed within sprayed areas in north Sacramento and unsprayed control zones in other urban–suburban locations in Sacramento and Yolo counties (Fig. 1). Data were summarized for 1-wk intervals pre- and postspray. Total trap nights were 26 and 20 in the spray zone and 26 and 29 in the unsprayed zone during the week before and the week after spray, respectively. Apart from three trapping records obtained from the data base of SYMVCD, all mosquito trapping in the spray zone was done in fixed locations that were used consistently in the week before and the week after spraying. In contrast, all data from the unsprayed zone were obtained from the routine mosquito and encephalitis virus surveillance done at the same period by technicians at SYMVCD. In this surveillance, $CO_2$-baited traps were placed randomly in different locations within control zones in Sacramento and Yolo counties. For the purpose of our study, we used all unsprayed zones' trapping data that occurred in urban–suburban locations that had a similar habitat as the north Sacramento Spray zone. All data were expressed as mosquito number per trap night. These numbers were either retrieved directly from the records of the sites that had one trap per night or obtained by dividing total number of mosquitoes by number of traps used per site per night. For analysis, mosquito numbers per trap per night were transformed by $\ln(y + 1)$ to normalize the distribution and control the variance and expressed as geometric or back transformation mean of weekly numbers for *Cx. tarsalis* and *Cx. pipiens* in sprayed and unsprayed zones. The formula described by Mulla et al. (1971) was used to calculate percent reduction of *Cx. tarsalis* and *Cx. pipiens* abundance in the week after intervention. In addition, factorial two-way analysis of variance (ANOVA) was used, within SPSS version 14 software (SPSS Inc., Chicago, IL), to test for significant changes in mosquito abundance in sprayed and unsprayed zones, before and after the spraying.

Mosquitoes from the traps described above and from traps placed in the spray zone and unsprayed areas at 2 wk before and 2 wk after the application of insecticide were pooled into lots of ≤50 females each, and then they were tested for WNV, St. Louis encephalitis, and western equine encephalomyelitis virus RNA by using a real-time multiplex reverse transcriptase-polymerase chain reaction (RT-PCR) (Brault et al., unpublished). WNV infection rates in mosquitoes were estimated using the bias-corrected maximum likelihood estimate (MLE) described by Biggerstaff (2006). Methods described by Biggerstaff (2008) were used to compute 95% confidence intervals (CI) for the differences of infection rates in the two areas before and after the application of insecticide.

## Results

Sentinel mosquitoes placed under different levels of canopy and wind shadow conditions during the first aerial spray showed variable mortality (Fig. 2). Greatest mortality was encountered in cages placed in open fields (100% in each cage), whereas the lowest rates occurred in sentinel cages placed along the bank of a dry creek under dense canopy and between buildings of a residential site. The overall mortality among mosquitoes placed in exposed or partially exposed sites (172/223 = 77.1%) was significantly higher than mortality of mosquitoes placed in protected places (62/250 = 24.9%; $\chi^2 = 129.1$, df = 1, $P < 0.001$). Although the actual counting of dead and live mosquitoes was performed at 12 h after spraying, we noticed that in the nine cages with 100% mortality rates all mosquitoes were dead 30 min after the spraying. This represented 78.2% (183/234) of the total number of dead mosquitoes in all cages. Immediate mortality at 30 min after spraying also was observed in the remaining cages with partial mortality rates. However, it was difficult to estimate the level of early mortality in these cages, because of the presence of live mosquitoes.

Comparing mosquito abundance measured during 1 wk before with 1 wk after spray, *Cx. pipiens* and *Cx. tarsalis* abundance was reduced by 75.0 and 48.7%, respectively (Table 1). The reduction in both species combined was 57.5%. Two-way ANOVA showed that mean *Cx. pipiens* abundance was significantly affected by the spray, as indicated by the significant interaction between time before and after treatment in the sprayed and unsprayed zones ($F = 4.965$; df = 1, 47; $P = 0.031$). In contrast, mean *Cx. tarsalis* abundance in the spray zone was not significantly reduced compared with the unsprayed zone ($F = 0.754$; df = 1,47; $P = 0.390$).

WNV infection rates in *Cx. pipiens* and *Cx. tarsalis* in the 2 wk before and the 2 wk after the insecticide application are shown in Table 2. Because of the small number of mosquito pools tested we were not able to

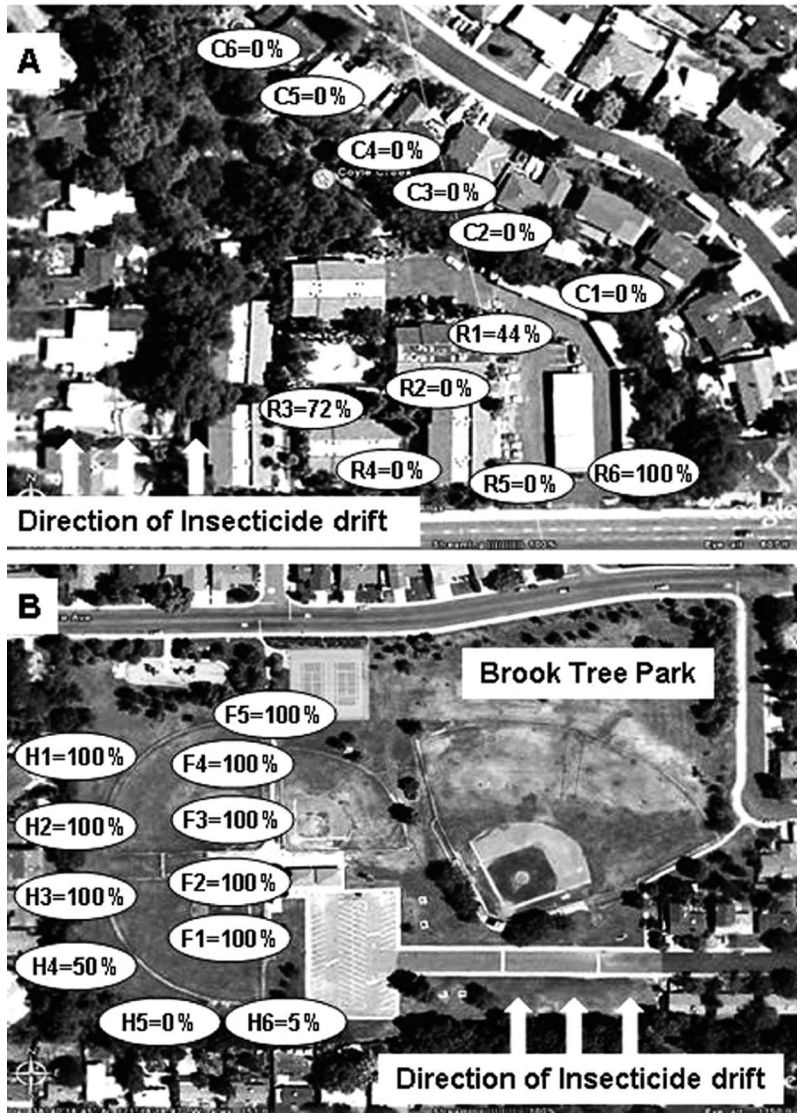


**Fig. 2.** Mortality rates (%) of mosquitoes held in bioassay cages (sentinel cages) and subjected to aerial spraying of pyrethrin insecticides in Coyle Creek and Brook Tree Park areas of north Sacramento, CA, 8 August 2005; (A) Cages held under dense canopy on the banks of Coyle Creek (C) and between buildings of an apartment complex (R). (B) Cages held under hedges of trees (H) and an open field (F) in Brook Tree Park. Arrows show direction of insecticide spraying. Maps were based on screenshots from Google Earth Mapping Service (http://earth.google.com).

determine the infection rates for each species independently. Using data for the two species combined, the overall infection rates in the spray zone were 8.2/1,000 (95% CI, 3.1–18.0/1,000) before spray and 4.3/1,000 (95% CI, 0.3–20/1,000) female mosquitoes after spray. Only a single positive pool was collected from the intervention zone, in the second week after spraying. In contrast, WNV infection rates in the same time intervals in the unsprayed areas were 2.0/1000 (95% CI, 0.1–9.7/1,000) and 8.7/1000 (95% CI, 3.3–18.9 /1000) females, respectively. It seemed that the infection rate in the spray zone decreased by 3.9/1,000 females (95% CI of prepost spray difference, −12.9–15.2/1,000), whereas it increased by 6.7/1,000 females (95% CI of prepost spray difference, −17.3–2.6/1,000) in the unsprayed areas. However, these differences were not statistically significant, as indicated by the overlap of the null value 0 by the 95% confidence intervals.

## Discussion

Although most guidelines for protecting the public during outbreaks of mosquito-borne encephalitis recommend aerial adulticiding as the most effective method of rapidly eliminating infective mosquitoes

**Table 1. Effects of aerial spraying of pyrethrin insecticide on abundance of *Cx. pipiens* and *Cx. tarsalis* in north Sacramento, CA, during the week before and after spray in August 2005**

| Sampling area | Sampling period in relation to spraying | No. trap nights | Geometric mean no. (confidence intervals) of mosquitoes per trap night | | |
|---|---|---|---|---|---|
| | | | *Cx. pipiens* | *Cx. tarsalis* | Total |
| Sprayed | Before | 26 | 7.4 (5.2–10.2) | 3.4 (1.8–5.9) | 11.0 (7.4–16.1) |
| | After | 20 | 3.7 (1.7–7.1) | 1.1 (0.3–2.4) | 4.6 (2.0–9.5) |
| Unsprayed | Before | 26 | 2.0 (0.6–4.4) | 4.8 (3.1–7.0) | 8.1 (5.3–12.3) |
| | After | 29 | 4.0 (1.8–7.8) | 2.9 (1.3–5.7) | 8.1 (4.2–14.9) |
| % control[a] | | | 75.0 | 48.7 | 57.5 |

[a] The % control value was calculated using the formula described by Mulla *et al* (1971). Values in parentheses show 95% CI of the mean.

and interrupting transmission (Mount et al. 1996, Moore et al. 2002, California Department of Health Services 2007), there are surprisingly few published studies measuring the impact of this control method on transmission in residential areas, especially in the United States. Our results indicated that the aerial spraying of pyrethrin in north Sacramento significantly reduced mosquito abundance and the number of infective bites received by human population. These results may explain the significant reduction of human cases and the interruption of the WNV epidemic in Sacramento that was reported by Carney et al. (2008). The analysis conducted by these authors indicated that the aerial spraying of north and south Sacramento resulted in an approximately six-fold decrease in the relative risk of infection in humans. They showed that after spraying, there were no new human WNV cases in either of the treated areas, whereas 18 new cases occurred in adjacent untreated areas in Sacramento County. In each of the sprayed areas, the proportions of pretreatment versus posttreatment cases were also significantly lower than untreated areas (Carney et al. 2008).

It is interesting that the aerial spraying of the insecticide significantly reduced the abundance of *Cx. pipiens* but not *Cx. tarsalis.* As suggested by Nielsen et al. (2007), these differences may be due to the location of the larval development sites of these mosquito species. *Cx. pipiens* usually breeds in urban–suburban locations, whereas *Cx. tarsalis* develops in rural agricultural sites such as the rice, *Oryza sativa* L., fields adjacent to Sacramento (Wekesa et al. 1996) and immigrates into town. Alternatively, these differences may be due to differences in their abundance in the sprayed and unsprayed areas and natural changes in their population densities during the time of spraying. It is noteworthy that the two species have marked differences in their seasonality in Sacramento County. After a decline in July, *Cx. pipiens* abundance usually continues to increase through August, reaching a peak in September (SYMVCD, unpublished data). In contrast, the population of *Cx. tarsalis* typically declines sharply by the end of July. Therefore, the insecticide application in the second week of August was impacting an increasing population of *Cx. pipiens* and an already declining population of *Cx. tarsalis.* Interestingly, *Cx. pipiens* was the primary vector of the 2005 WNV epidemic in the area (Elnaiem et al. 2006). In 2005, the total WNV infection rate in this species in Sacramento and the neighboring Yolo counties (5.3/

**Table 2. Weekly infection rates of WNV in *Culex* mosquitoes collected from areas that were subjected to aerial spraying of pyrethrin insecticide and other unsprayed areas in Sacramento and Yolo counties, CA, July–August 2005[a]**

| Location | Sampling period | No. females | No. pools | No. +ve pools | % +ve pools | MLE[b] (95% CI) |
|---|---|---|---|---|---|---|
| North Sacramento spray area | Pretreatment | | | | | |
| | 24–31 July | 354 | 12 | 4 | 33.3 | 11.9 (4.2–28.3) |
| | 1–7 Aug. | 297 | 23 | 1 | 4.3 | 3.4 (0.2–16.9) |
| | Total | 651 | 35 | 5 | 14.3 | 8.2 (3.1–18.0) |
| | Posttreatment | | | | | |
| | 11–15 Aug. | 145 | 19 | 0 | 0 | 0 |
| | 16–23 Aug. | 85 | 11 | 1 | —[c] | —*3 |
| | Total | 230 | 30 | 1 | 3.3 | 4.3 (0.3–20.3) |
| Unsprayed areas | Pretreatment | | | | | |
| | 24–31 July | 211 | 9 | 0 | —[c] | —[c] |
| | 1–7 Aug. | 284 | 9 | 1 | —[c] | —[c] |
| | Total | 495 | 18 | 1 | 5.6 | 2.0 (0.1–9.7) |
| | Posttreatment | | | | | |
| | 8–15 Aug. | 346 | 21 | 4 | 19.0 | 12.1 (4.2–28.6) |
| | 16–23 Aug. | 251 | 28 | 1 | 3.6 | 3.9 (0.2–18.5) |
| | Total | 597 | 49 | 5 | 10.2 | 8.7 (3.3–18.9) |

[a] Aerial spraying on 8–10 Aug. 2005.

[b] Bias-corrected maximum likelihood estimate of infection rate/1,000 mosquitoes (Biggerstaff 2006); 95% CI based on skewness-corrected statistic.

[c] No calculation of percentage of number of positive pools or estimation of infection rates were made, due to small number of individuals and pools examined.

1,000; 95% CI, 3.8–7.2/1,000) was more than double the infection rate detected in *Cx. tarsalis* (2.03/1000; 95% CI, 1.4–2.8/1,000) (SYMVCD, unpublished data). Furthermore, *Cx. pipiens* was predominantly the most abundant urban vector of WNV, accounting for 66.8% (2,654/3,976) of all *Culex* mosquitoes captured in $CO_2$-baited traps placed in the residential areas of north and south Sacramento, where the epidemic occurred. Thus, control of *Cx. pipiens* was of greatest importance, and the significant reduction of the abundance of this species should have a strong impact on the WNV epidemic despite the absence of a significant reduction in *Cx. tarsalis* populations.

The sentinel mosquito protocol adopted in our study differed from protocols used in other studies in that mosquitoes were not transferred to new unexposed holding cages after the spraying (Bunner et al. 1989). Our procedure may have resulted in an overestimation of mosquito mortality rates by increasing their continued exposure to pesticide residues on the cages; however, results from previous trials (G.Y., unpublished) where a portion of the mosquitoes were transferred indicated minimal differences that were offset by the disadvantages of mosquito trauma from handling and transfer to new cages. Furthermore, the observation that most mosquitoes died immediately after spraying indicates that the effects of increased mortality due to continued exposure to the insecticide residues in the cages did not have a substantial influence on our results. Our results indicate that in some places the impact of the aerial spraying was affected by the wind shadow effects caused by residential buildings and dense vegetation. ULV particles apparently did not effectively contact sentinel mosquitoes placed within an apartment complex, under dense tree canopy or along the banks of a dry creek, areas often frequented by questing females. Similar results were reported recently for aerial applications in neighboring Davis in Yolo County (Nielsen et al. 2007).

The rationale for adulticiding during epidemics of mosquito-borne diseases is to reduce the number of infected mosquitoes and thus interrupt pathogen transmission. Depending on its efficacy and the number of newly emerging adults, adulticiding may also result in a reduction in mosquito infection rates by affecting the age structure of the mosquito population. Due to the small number of mosquito pools collected from the sprayed and unsprayed areas at each time interval, we were not able to determine the infection rates in each species of mosquitoes separately. This limitation may have some consequences on the interpretation of the impact of aerial spraying on the infection rates of WNV, because different species may be impacted differently and their infection rates may fluctuate depending on their ecology and behavior. Our findings that the reduction in the combined infection rates was not statistically significant are considered inconclusive however, because of the small sample sizes of the mosquito pools which generated large 95% confidence intervals.

Even without a significant change in the infection rate, we suggest that the significant reduction in the abundance of *Cx. pipiens* resulted in a decrease in the number of infective bites received by the human population and consequently impacted the transmission of the disease. It must be stressed that the vectorial capacity, or force of transmission, of vector-borne pathogens (MacDonald 1957; Garrett-Jones 1964), is highly dependent on the biting rate, which is also dependent on vector abundance. Based on this justification, we conclude that the aerial spraying of pyrethrin insecticide in north Sacramento resulted in interruption of WNV transmission and reduced the risk of human infection. Nonetheless, and considering the environmental and health hazards of pesticides, we emphasize that mosquito adulticiding should be used as part of a comprehensive intervention program, when surveillance indicates an increased risk of infection to humans.

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## Original Contributions

# THE EPIDEMIOLOGY OF ST. LOUIS ENCEPHALITIS IN DALLAS, TEXAS, 1966

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**Hopkins, C. C., F. B. Hollinger, R. F. Johnson, H. J. Dewlett, V. F. Newhouse and R. W. Chamberlain (Center for Disease Control, Atlanta, GA 30333). The epidemiology of St. Louis encephalitis in Dallas, Texas, 1966. *Am J Epidemiol* 102:1-15, 1975.—An epidemic of St. Louis encephalitis (SLE) occurred in Dallas, Texas, in the summer of 1966. A total of 545 suspected cases within Dallas city and county were reported, of which 145 were laboratory-confirmed as SLE virus infection. The greatest concentration of cases occurred in lower socioeconomic areas of the central part of the city in black populations. The attack rate and mortality rate increased markedly with age. The overall attack rate was 15.2 per 100,000, with a case fatality rate of 9.7%. During the course of the epidemic, most of the county was sprayed aerially with an ultra-low volume (ULV), high-concentration malathion mist. The effects of this treatment cannot be adequately assessed from the human epidemiologic aspect alone, but the spraying clearly reduced the number and infection rate of the vector mosquitoes.**

**arbovirus infections; encephalitis, St. Louis; mosquito control**

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Abbreviations: CF, complement fixation; CNS, central nervous system; HAI, hemagglulination inhibition; MVE, Murray Valley encephalitis; SLE, St. Louis encephalitis; ULV, ultra-low-volume.

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## INTRODUCTION

St. Louis encephalitis (SLE) was first seen in epidemic proportion in the early 1930's (1, 2) and has since become recognized as a major urban hazard in certain parts of the United States. In the summer of 1966, an epidemic occurred in Dallas, Texas, which resulted in 145 cases of confirmed SLE virus infection and 14 deaths over an 11-week period. The outbreak was recognized early, permitting epidemiologic and laboratory investigations to be performed during its course to assess the efficacy of mosquito control efforts in prevention of disease. For the first time, control of urban SLE was attempted by aerial application of malathion with the ultra-low-volume (ULV) technique. This paper summarizes the epidemiologic findings of the investigation.

## BACKGROUND

Dallas is located on the northwestern corner of the Gulf Coastal Plain in rich prairie land with scattered low rolling hills. The Trinity River transects the city northwest to southeast and is separated from the central city on either side by a strip of bottom land about 305 meters wide, bounded by high levees.

The climate is temperate, with a moderate winter and a hot summer. The average annual rainfall is 89 cm. In 1966, however, unusually heavy rains occurred during the last week of April, causing floods in many areas. The total April rainfall was 39 cm, 29 cm in excess of normal; more than 30 cm of rain fell during April 22–25 and April 28–30 (3).

The natural water table is high in the city of Dallas. This excessive rainfall overloaded the drainage and sewage management system, causing back-up of water in the drains and creating pools of standing water enriched with organic waste favorable for mosquito breeding throughout the low-lying parts of the city.

No known cases of human infection with St. Louis encephalitis virus had occurred in Dallas before 1966, although the virus had been isolated from mosquitoes in adjoining counties. In the last week of July 1966, five patients with symptoms of encephalitis were admitted to Parkland Memorial Hospital in Dallas. Sera from these patients were sent to the State Health Department Laboratory in Austin; three of the five sera reacted with antigens prepared from several Group B arboviruses, including SLE, by the hemagglutination-inhibition (HAI) test. By August 8, a total of 14 patients with clinical encephalitis had been admitted to Parkland. On August 10, the Center for Disease Control (CDC), the Texas State Health Department and the Dallas Health Department initiated a cooperative program to investigate and control the epidemic.

## METHODS

*Investigation of human cases.* During the epidemic, suspect cases of central nervous system (CNS) disease were tracked down as follows: 1) With the assistance of the Dallas County Medical Society, all hospitals and physicians of Dallas County were contacted by mail and asked to report all cases of suspect CNS disease directly to the Dallas Health Department. 2) All hospitals in the county were contacted daily in person or by telephone for information on suspect CNS disease in patients admitted during the preceding 24 hours. 3) Serum specimens submitted to the Dallas Health Department for diagnostic testing for CNS disease or related illnesses were also reported to the investigating team. (Most of these specimens proved to be from patients already identified by the other methods.) 4) Public interest and medical concern were stimulated and maintained throughout the epidemic by daily publicity through TV, radio, and the press.

The adequacy of the reporting of suspected clinical cases of CNS disease was indicated by the relatively low percentage

of all reported cases which finally could be confirmed as related to SLE virus (see below). It appears likely that only those persons not ill enough to be attended by a physician or go to a hospital outpatient clinic remained uninvestigated.

Every reported case was studied clinically and epidemiologically by a member of the investigating team, and serum specimens were obtained at appropriate times for specific diagnostic studies.

*Clinical classification.* On the basis of a physical examination and a complete history, patients were placed in one of four clinical categories.

1) *Encephalitis.* This was defined as a serious febrile illness of unknown etiology, in which severe headache and signs of CNS involvement predominated. The diagnosis did not depend on the presence or absence of signs of meningeal irritation or cells in the spinal fluid. The signs of encephalitis most commonly seen in patients were tremor, ataxia, confusion, disorientation, or alterations in their state of consciousness.

2) *Aseptic meningitis.* Into this category were put the patients with clinical evidence of meningeal irritation (e.g., headache, fever and stiff neck) who failed to reveal clinical evidence of neuroparenchymal involvement. An exception was made when a lumbar puncture, performed early in the clinical course and adequately examined, showed fewer than five cells per $mm^3$ in the spinal fluid. In such instances, because clinical signs of meningeal irritation may occasionally be equivocal, the patient was assigned to the "febrile headache" category (see below). Patients with documented signs of meningeal irritation but whose spinal fluid had not been examined were left in the "aseptic meningitis" category.

3) *Febrile headache.* All persons with fever and headache who clearly did not have signs of meningeal irritation or abnormalities of neurologic function, regardless of spinal fluid cellularity, were placed in this category. If meningeal signs were present but no cells were found in the spinal fluid, the patient was included in this category.

4) *Other syndromes.* Patients whose symptoms fitted none of the above categories were classified as "other."

*Laboratory methods.* All sera were initially screened by the Texas State Department of Health Laboratory using the HAI technique to assay for activity against two Group B antigens, namely, SLE and Murray Valley encephalitis (MVE). MVE antigen is frequently used in Group B arbovirus serology because of its broad group reactivity which makes it an excellent screening reagent. Later, in both the Texas State Department of Health Laboratory and the Arbovirology Section of CDC, complement-fixation (CF) tests were conducted on these same sera. Serologic identification was confirmed by assaying for neutralizing antibodies. The methods involved in these serologic assessments have been outlined previously (4).

Viral isolation attempts (4) from pathologic specimens were performed by the late Dr. S. Edward Sulkin of the University of Texas Southwestern Medical School.

*Laboratory criteria.* On the basis of the laboratory data and independent of clinical evaluation, cases were divided into the following four categories:

1) *Confirmed.* a) Demonstration of at least a fourfold rise or fall in titer in paired serologic specimens (acute and convalescent) against SLE antigen as determined by the HAI or CF test. Because of the possibility of cross-reactions with other Group B arbovirus infections, a fourfold or greater rise in HAI titer against SLE antigen was considered confirmatory only after other Group B arboviruses had been excluded. b) Isolation of SLE virus from tissues. c) Histopathologic evidence of encephalitis together with an HAI titer of $\geq$1:320 or a CF titer of $\geq$1:16 in the ab-

sence of evidence of other Group B arbovirus infections.

2) *Presumptive.* An HAI titer of $\geq$1:10 against SLE in a patient in which further assessment was not possible because of an inadequate number or spacing of serum specimens.

3) *Inconclusive.* Failure to demonstrate HAI or CF antibody against SLE when the only serum specimens received were collected before the 10th day of illness. It is recognized that such a case might have either been confirmed or shown to be negative had further specimens been received.

4) *Negative.* a) Failure to demonstrate HAI or CF antibody against SLE in a serum specimen collected 10 or more days after onset of illness. b) Presence of measurable antibodies but failure to demonstrate a significant change in HAI or CF titers in appropriately spaced specimens against SLE antigen as described above. Such reactions were interpreted as representing past infections with SLE virus.

*Population data.* The population data used in the calculation of rates are from the 1960 US census for Dallas County. The socioeconomic status of the residents in each census tract was ranked by the Serfling-Sherman technique (5) according to percentage of sound housing, percentage of houses with more than one person per room, and median school year completed by the head of the household. By this method the upper socioeconomic section had 25 per cent of the total population of the county and the lower section comprised 25 per cent. The remaining 50 per cent of the population was divided evenly between upper-middle and lower-middle socioeconomic sections. In additional geographic analyses the county was divided into groups of census tracts and comparative rates were calculated.

From examination of selected areas of the county, it was obvious that extensive shifts in population had taken place since 1960. Although estimates made in 1964 of total population were available by census tract, no similar estimates for racial and socioeconomic groups existed, which precluded accurate calculations of rates within these population groups.

*Investigation of mosquito vectors.* Commencing on August 10 and continuing until late October, daytime collections of resting mosquitoes were made regularly from up to 38 separate sites throughout the city. The collections were made by hand, using aspirators (6). A wide variety of habitats was represented, including back-yard chicken coops, garages, sheds, porches, culverts, and the undersides of houses and bridges. This method of sampling favored the collection of *Culex quinquefasciatus* Say, the established urban vector of SLE in the south-central part of the United States. The mosquitoes collected daily were sorted, tabulated according to collection site, preserved by freezing on Dry Ice, and sent to the Arbovirology Section, CDC, where they were promptly identified, pooled, and tested for virus by standard methods (6).

The mosquito vector control program consisted of ULV application of 95 per cent malathion at the rate of approximately 225 ml per hectare by low-flying US Air Force C-123 Globemaster aircraft. This program has been summarized elsewhere (7). This type of treatment is highly effective for killing adult mosquitoes, but it does not generally reduce the existing larval mosquito population. During an epidemic, however, the prime thrust should be to eliminate the infected adult mosquitoes as quickly as possible. For this purpose, the ULV method is ideal. A total of approximately 1927 $km^2$ of Dallas city and county were sprayed between August 19 and 27 during seven days of spray operation.

Supplementary ground control was also carried out in various parts of the city by fogging with 2 per cent malathion in diesel oil or dusting with commercial prepara-

tions containing 3 per cent benzene hexachloride or 5 per cent malathion.

Prior to August 19 the ground treatment measures were the only mosquito control measures locally available, and they undoubtedly served to reduce the adult mosquito populations close to the areas of application. It is quite likely that they may have prevented additional human exposures from occurring in heavily infected neighborhoods, but the vector sampling methods used were inadequate to assess this.

## Results

During the course of the epidemic (July 13 to September 25) 545 cases of suspected CNS disease in Dallas County were reported. These included 182 cases of clinical encephalitis, 114 cases of aseptic meningitis, 114 cases of febrile headache, and 135 cases of other syndromes. A total of 145 cases of SLE (26.6 per cent) were confirmed by the laboratory criteria described above, for a case rate for Dallas County of 15.2 per 100,000. Of these 145 cases, 119 were clinically classified as encephalitis, 13 as aseptic meningitis, 6 as febrile headache, and 7 as other syndromes, as shown in table 1. The following description of the human epidemiology considers only the *confirmed* cases, clearly attributed to recent infection with SLE virus. When only confirmed cases are considered, the Dallas epidemic can be directly compared with a concurrent epidemic in Corpus Christi (8) where interpretation of "presumptive" results was obscured by antibody resulting from known prior SLE virus activity.

Descriptions of previous urban epidemics of SLE have used a somewhat broader definition of a "case" (9, 10). To permit direct comparison of our data with those from earlier outbreaks, it is necessary to include the additional 27 "presumptive" cases (a total of 172 confirmed and presumptive cases combined). Based on the 172 case figure, the attack rate in Dallas was 18.1 per 100,000 population. The epidemiologic characteristics of the 27 "presumptive" cases do not differ substantially from those of the 145 confirmed cases described below.

The earliest reported and confirmed SLE illnesses in Dallas had onset in the second week of July, a time which can be taken as the beginning of the epidemic. Only seven cases were reported in the first 17 days of the epidemic. In the first week of August, however, the total number of reported cases greatly increased; then in the third week of August, the number of new cases began to decline gradually (figure 1). The last confirmed case had onset on September 24. The epidemic lasted 11 weeks.

As shown in table 2, attack rates were

Table 1

*St. Louis encephalitis, Dallas County, July 13–September 25, 1966, clinical and laboratory classification, all reported cases*

| Laboratory category | Clinical category | | | | |
|---|---|---|---|---|---|
| | Encephalitis | Aseptic meningitis | Febrile headache | Other | Total |
| Confirmed | 119 | 13 | 6 | 7 | 145 |
| Presumptive | 16 | 3 | 5 | 3 | 27 |
| Inconclusive | 4 | 4 | 4 | 19 | 31 |
| Negative | 43 | 94 | 99 | 106 | 342 |
| Total | 182 | 114 | 114 | 135 | 545 |

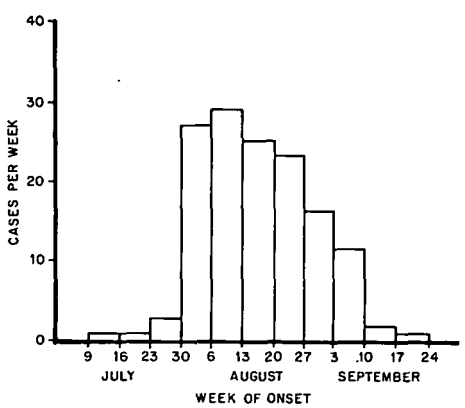


Figure 1. St. Louis encephalitis, Dallas County, 1966, 145 confirmed cases, by week of onset.

TABLE 2

*St. Louis encephalitis, Dallas County, 1966, age-specific attack rates, mortality rates,* and case-fatality ratios*

| Group | Population* | Cases | Attack rate/ 100,000 | Deaths | Mortality rate/100,000 | Case/fatality ratio (%) |
|---|---|---|---|---|---|---|
| 0–9 | 221,764 | 13 | 5.9 | | | |
| 10–19 | 148,183 | 10 | 6.7 | | | |
| 20–29 | 133,393 | 8 | 6.0 | | | |
| 30–39 | 147,793 | 21 | 14.2 | | | |
| 40–49 | 119,964 | 18 | 15.0 | 1 | 0.8 | 6.1 |
| 50–59 | 88,879 | 26 | 29.3 | 2 | 2.3 | 7.7 |
| 60–69 | 54,770 | 27 | 49.3 | 5 | 9.1 | 18.5 |
| 70+ | 36,781 | 22 | 59.9 | 6 | 16.3 | 27.3 |
| Total | 951,527 | 145 | 15.2 | 14 | 14.7 | 9.7 |

* 145 confirmed cases; population data—US Census, 1960.

progressively higher in the older age groups, reaching a high of 59.9 cases per 100,000 in persons over 70 years of age. In no age group was there a significant difference in incidence by sex. A greater proportion of cases in the older age groups had clinical symptoms of encephalitis (table 3): 54 per cent of patients under 10 years of age with confirmed cases had symptoms of encephalitis, whereas 95 per cent of the patients over 70 years of age had these symptoms.

The incidence in the black population (37.1 per 100,000) was significantly higher than in the white population (11.4 per 100,000) (table 4). Attack rates were also significantly higher in areas of lower socioeconomic status (table 5). We feel that geographic factors, described below, were predominantly involved; and we are reluctant, in the absence of more current detailed population data, to critically compare attack rates in regard to either race or socioeconomic status.

Figure 2 shows the geographic distribution of the known residences of 142 of the patients with confirmed SLE. As the epidemic began, one cluster of cases appeared southwest of the Trinity River in the south-central part of town. Cases were soon found widely scattered throughout the city, primarily in areas with lower socioeconomic black populations but also including the outlying suburbs. However, despite intensive surveillance, only one case was noted in the extreme northeast area of the county. The concentration of cases in the center of the city is not simply a function of population concentration; grouped census tracts in the center of the city had higher attack rates than grouped census tracts in the periphery (table 6). As shown in table 7, north of the Trinity River the attack rate (11.3 per 100,000) was significantly lower than the rate south of the Trinity River (21.5 per 100,000) ($p < 0.01$). South of the river, the respective attack rates among both white and black residents were higher than those north of the river, which suggests that risk was indeed a function of geographic location, although the lack of recent population data makes further analysis of these subgroups unre-

TABLE 3

*St. Louis encephalitis, Dallas County, 1966, distribution of clinical syndromes by age**

| Age | Encephalitis | Aseptic meningitis | Febrile headache | Other | Total |
|---|---|---|---|---|---|
| 0–9 | 7 | 6 | | | 13 |
| 10–19 | 9 | 1 | | | 10 |
| 20–29 | 5 | 3 | | | 8 |
| 30–39 | 15 | 3 | 2 | 1 | 21 |
| 40–49 | 16 | | 1 | 1 | 18 |
| 50–59 | 22 | | 2 | 2 | 26 |
| 60–69 | 24 | | 1 | 2 | 27 |
| 70+ | 21 | | | 1 | 22 |
| Total | 119 | 13 | 6 | 7 | 145 |

* 145 confirmed cases.

TABLE 4

*St. Louis encephalitis, Dallas County, 1966, attack rates, mortality rates, and case-fatality ratios by race**

| Race | Population* | Cases | Attack rate per 100,000 | | Deaths | Mortality rate/100,000 | Case-fatality ratio |
|---|---|---|---|---|---|---|---|
| | | | Not age-adjusted | Age-adjusted† | | | |
| White | 811,261 | 93 | 11.4 | 10.9 | 7 | 0.9 | 7.5 |
| Black | 140,266 | 52 | 37.1 | 41.3 | 7 | 5.0 | 13.5 |
| Total | 951,527 | 145 | 15.2 | | 14 | 1.5 | 9.7 |

* 145 confirmed cases; population data—US Census, 1960.

† Age adjustments made on the basis of age distributions for the total Dallas County population, 1960 Census.

TABLE 5

*St. Louis encephalitis, Dallas County, 1966, attack rate by socioeconomic status of area of residence**

| Socioeconimic status† | Population | Cases | Attack rate per 100,000 | |
|---|---|---|---|---|
| | | | Not age-adjusted | Age-adjusted |
| Upper | 240,072 | 11 | 4.6 | 4.3 |
| Upper-middle | 237,072 | 25 | 10.5 | 10.7 |
| Lower-middle | 236,374 | 54 | 22.8 | 23.0 |
| Lower | 238,009 | 52 | 21.8 | 23.4 |
| Total | 951,527 | 142 | 14.9 | |

* Includes 142 confirmed cases with known location of residence; population data—US Census, 1960.

† Socioeconimic status of area of residence calculated by Serfling-Sherman technique (see text).

liable. In 1960, however, the socioeconomic status of the population north of the river was somewhat higher than that in the south, although the proportionate racial distribution of these areas was similar.

*Mortality.* Thirty-four deaths occurred among all reported suspect cases. Twenty of these 34 deaths could have been due to causes other than SLE virus infection. Seven of these 20 had no serologic evidence of SLE and were clearly related to other diseases. Three patients with presumptive SLE virus infection almost certainly died as a result of other medical conditions, and one patient with serologically confirmed SLE died from a dissecting aneurysm. Another patient who died had inconclusive serologic results on a single blood sample obtained postmortem 4 days after onset of illness. Eight other persons with presumptive cases died.

Among the 145 confirmed SLE virus infections, 14 deaths were clearly related to this illness alone, giving a mortality rate in Dallas County of 1.5 per 100,000 and a case fatality ratio of 9.7 per cent (table 4). Of the 14 patients who died, 13 had a clinical diagnosis of encephalitis, while one had a focal paralytic disease without other encephalitis symptoms and was classified in the "other syndrome" category.

The youngest patient to die was a 45-year-old man with severe underlying alcoholic disease, but the majority of persons who died were over 70, for a case fatality ratio of 27.3 per cent for this age group (table 2). There was no difference in mortality between sexes. As shown in table 4, the mortality rate was higher in the black population, but this reflects the higher attack rates in this group. In fact, the case fatality ratio for the black population (13.5 per cent) was not significantly different from that for the white population (7.5 per cent), ($p$ = 0.40).

*Control measures and vector assessment.* After the spring rains and flooding, 3 per cent benzene hexachloride dust had been applied by ground-operated equipment throughout the parts of the city most heavily affected by the floods. The results of this type of treatment in the control of expected mosquito breeding were not fully evaluated; however, it is apparent that such treatment immediately after flooding

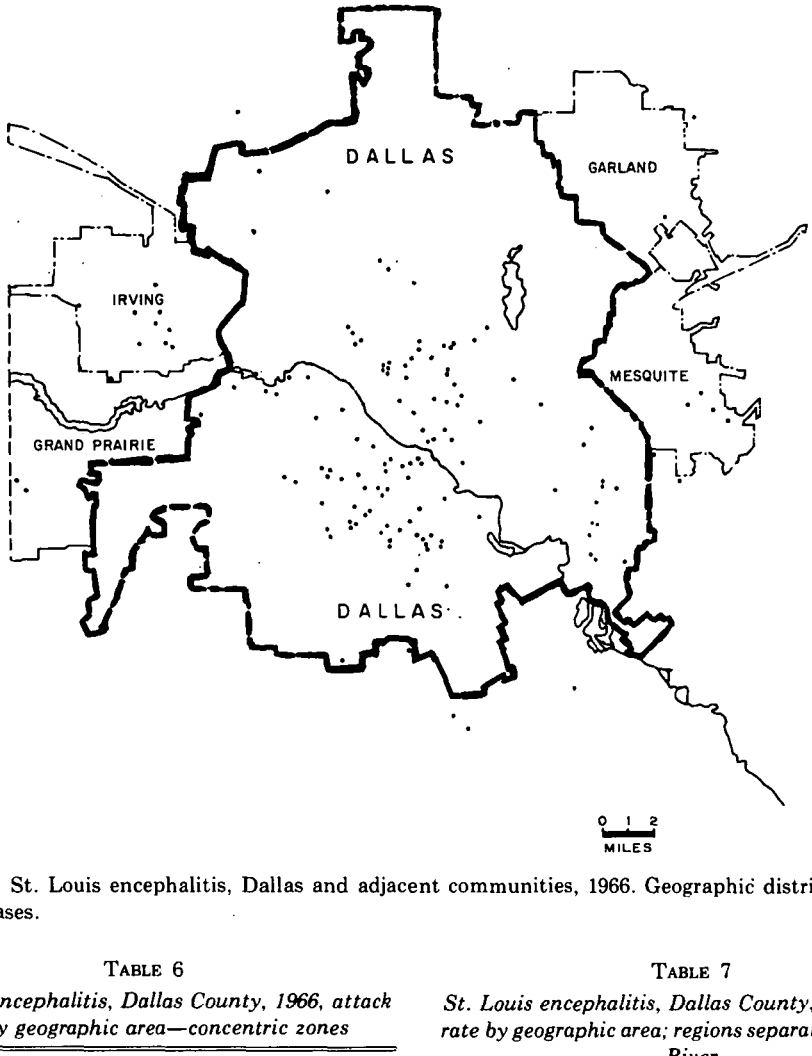


FIGURE 2. St. Louis encephalitis, Dallas and adjacent communities, 1966. Geographic distribution of 142 confirmed cases.

TABLE 6

*St. Louis encephalitis, Dallas County, 1966, attack rate by geographic area—concentric zones*

| Distance from center | Population* | Cases | Attack rate per 100,000 | |
|---|---|---|---|---|
| | | | Not age-adjusted | Age-adjusted |
| <1.6 km | 260,417 | 64 | 24.5 | 21.6 |
| 1.6–3.2 km | 389,463 | 49 | 12.6 | 12.7 |
| >3.2 km | 301,647 | 29 | 9.6 | 11.9 |
| Total | 951,527 | 142 | 14.9 | |

* Grouped census tracts within each concentric zone.

TABLE 7

*St. Louis encephalitis, Dallas County, 1966, attack rate by geographic area; regions separated by Trinity River*

| Zone | Population | Cases | Attack rate per 100,000 | |
|---|---|---|---|---|
| | | | Not age-adjusted | Age-adjusted |
| North | 603,427 | 68 | 11.3 | 11.1 |
| South | 297,538 | 64 | 21.5 | 21.6 |
| West | 50,562 | 10 | 19.8 | 25.0 |
| Total | 951,527 | 142 | 14.9 | |

is much more effective in reducing the numbers of flood-water pest mosquitoes, such as various species of *Aedes* and *Psorophora*, than of the urban SLE vector, *C. quinquefasciatus*. It is in the long aftermath of flood conditions that the water catchments become most favorable for the breeding of this vector species, when evaporation has caused a concentration of the contained organic pollutants.

With the onset of cases of human encephalitis, fogging and dusting trucks were

dispatched to affected neighborhoods in attempts to reduce the numbers of infected vector mosquitoes. Meanwhile, political and technical arrangements were made to permit aerial ULV spraying of the entire city of Dallas and most of the county, as earlier mentioned under "Methods." The areas covered during seven days of aerial spray operation between August 19 and 27 are shown in figure 3. Mosquito sampling in resting sites was carried out before and after aerial spraying with a threefold purpose: to determine the vector species involved, to determine their SLE virus infection rates (ratio of individual adult female mosquitoes infected), and to estimate changes in vector population density. The sampling sites were widely distributed throughout the city but were somewhat more concentrated in the low-lying areas near the Trinity River than in the more elevated outskirts. About 15–20 collection sites were involved in the sequential sampling during the pre-spray period. These were gradually increased to 38 sites in the post-spray period.

The only mosquito species taken in large numbers in Dallas was *C. quinquefasciatus*, the suspected vector (table 8). It was undoubtedly the most abundant mosquito in Dallas. There was a strong likelihood that the severe floods between April 22 and May 5 provided conditions favoring greater midsummer breeding of *C. quinquefasciatus* than usual. The fact that there were larger catches of *C. quinquefasciatus* than of other mosquito species was also a reflection of the biased method of mosquito collection used, i.e., hand-catching (aspirating) from various daytime resting places.

The mosquitoes collected in the resting sites are listed in table 8 according to species and week of collection. Since this

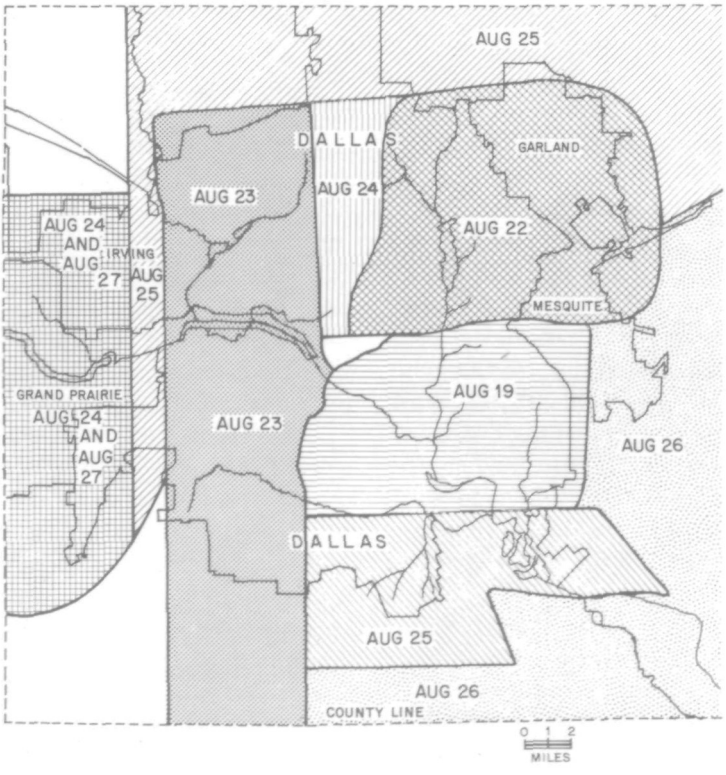


FIGURE 3. St. Louis encephalitis, Dallas County, 1966. Aerial spraying, by area and date.

TABLE 8

*Mosquitoes collected during periodic inspections of daytime resting sites in Dallas, Texas, 1966*

| Species | Numbers of mosquitoes caught by week of collection* | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Aug 7–13 | Aug 14–20 | Aug 21–27 | Aug 28–Sep 3 | Sep 4–10 | Sep 11–17 | Sep 18–24 | Sep 25–Oct 1 | Oct 2–8 | Oct 9–15 | Oct 16–22 | Oct 23–29 | Total |
| *Aedes* species† | 100 | 53 | 17 | 1 | 3 | 1 | | 2 | 3 | | | | 180 |
| *Anopheles* | | | | | | | | | | | | | |
| *quadrimaculatus* | 31 | 28 | 54 | 18 | 47 | 58 | 147 | 131 | 104 | 84 | 47 | 50 | 799 |
| other species‡ | 4 | 16 | 12 | 1 | 1 | 7 | 7 | 12 | 7 | 29 | 11 | 23 | 130 |
| *Culex* | | | | | | | | | | | | | |
| *(Mel.) sp.* | 128 | 103 | 83 | 26 | 38 | 90 | 47 | 68 | 59 | 106 | 46 | 89 | 883 |
| *quinquefasciatus* | 3495§ | 4272 | 3121 | 4343 | 4647 | 8124 | 7288 | 7962 | 7603 | 4137 | 6459 | 6119 | 67570 |
| *tarsalis* | 15 | 2 | 44 | 12 | 46 | 69 | 206 | 177 | 37 | 14 | 25 | 10 | 657 |
| other species‖ | 39 | 118 | 1 | 1 | 2 | 6 | 4 | 14 | 4 | 27 | 5 | 9 | 230 |
| Minor genera¶ | 6 | 1 | | 1 | 3 | 5 | | 4 | 1 | 4 | 5 | 5 | 35 |
| Total mosquitoes | 3818 | 4593 | 3332 | 4403 | 4787 | 8360 | 7699 | 8370 | 7818 | 4401 | 6598 | 6305 | 70484 |
| No. of site inspections | 9 | 47 | 100 | 156 | 65 | 140 | 117 | 113 | 78 | 108 | 95 | 106 | |
| Mean mosquitoes per site inspection | 424 | 98 | 33 | 28 | 74 | 60 | 66 | 74 | 100 | 41 | 69 | 59 | |

* The mosquitoes were tested for virus in 3172 pools by intracerebral inoculation of suckling mice.

† *Aedes* species and total numbers taken: *aegypti*, 4; *sollicitans*, 2; *taeniorhynchus*, 3; *triseriatus*, 2; *vexans*, 169.

‡ Minor *Anopheles* species and total numbers taken: *barberi*, 3; *crucians*, 3; *pseudopunctipennis*, 1; *punctipennis*, 123.

§ Weekly collections underlined yielded isolations of SLE virus; refer to tables 9 and 10.

‖ Minor *Culex* species and total numbers taken: *restuans*, 53; *salinarius*, 163; *territans*, 14.

¶ Minor genera and species, total numbers taken: *Culiseta inornata*, 14; *Mansonia perturbans*, 1; *Psorophora confinnis*, 15; *Psorophora ferox*, 1; *Uranotaenia sapphirina*, 4.

table is not organized by area according to pre-spray or post-spray time of mosquito collection, it does not show the effects of the control efforts to best advantage. The aerial spraying began on August 19, and more than a week was required to cover the entire city; this control lag tended to obscure the sharp reduction in mosquitoes that actually occurred in each area sprayed. Nonetheless, beginning with the week of August 21, a sharp drop-off is seen in the average number of mosquitoes captured per site inspection, despite the overlapping counts from still unsprayed areas.

The effectiveness of the spray operation is more clearly shown in figure 4, where the daily mean mosquito collection counts are plotted according to spray date. It is evident from this chart that immediately after spraying, the resting site counts dropped to near zero for about a week. These reduced counts can be assumed to reflect a similar reduction in the total adult mosquito population throughout the sprayed areas. Such mass killing of vector mosquitoes, infected and noninfected alike, is enough to temporarily reduce transmission to an ineffectual level. Furthermore, since SLE viremia usually occurs in birds within 18 to 48 hours after infected mosquito bite, and usually lasts no longer than 3 or 4 days, it is apparent that most, if not all, of the infected birds had time to lose their viremia before the succeeding crop of mosquitoes emerged. It is likely that the infection cycle, if not actually broken, was indeed significantly impeded by this combined action of vector reduction and reduced virus source.

Concurrent bird studies (11) revealed significant rates of SLE antibody in all major species of birds, indicating that infections had been widespread. The antibody rate in house sparrows was especially high, and in view of the superabundance of this species in the affected areas, it was estimated to have been by far the most available virus source for infection of mosquitoes. The sparrow's close association with man and in turn with the primary

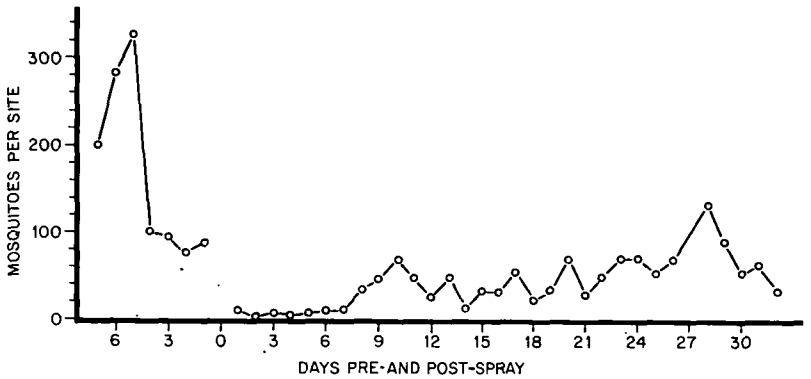


FIGURE 4. Mosquito collections from daytime resting sites, Dallas, 1966. Weighted daily mean mosquito count per site, plotted by day of aerial spray treatment.

vector species, the peridomestic *C. quinquefasciatus*, further suggests the importance of its position in the disease cycle.

The number of isolations of SLE virus made from *C. quinquefasciatus* and *Culex tarsalis* are given by week of collection in table 9. These were the only species of mosquitoes found infected with SLE virus during the Dallas outbreak. *C. tarsalis* is an important vector of SLE and western equine encephalitis farther west, but was apparently relatively unimportant as an SLE vector in Dallas. It did not appear in appreciable numbers until mid-September, as shown in table 8. By then the epidemic was essentially over.

Table 10 lists the SLE virus isolations from the main vector, *C. quinquefasciatus*, according to spray date for area of collection, and thus is a companion for figure 4. It also presents the infection rates of this species by spray date. In the calculation of the pre-spray infection rate, the 0- and 1-day post-spray mosquitoes were included with the pre-spray group. This was done because they really represented pre-spray mosquitoes which were either collected before the spray had time to take effect or before they had time to disperse. Approximately 10,000 *C. quinquefasciatus* mosquitoes were collected during the pre-spray and 0-1 day samplings. From these, 62 isolations of SLE virus were made, for an

TABLE 9

*Isolations of St. Louis encephalitis virus from mosquitoes, Dallas, Texas, 1966*

| Week of mosquito collection | No. SLE virus isolations/No. mosquitoes tested | |
|---|---|---|
| | *C. quinquefasciatus* | *C. tarsalis* |
| Aug 7–13 | 29/3,495 | 0/15 |
| Aug 14–20 | 22/4,272 | 0/2 |
| Aug 21–27* | 11/3,121 | 0/44 |
| Subtotals | 62/10,888 | 0/61 |
| Aug 28–Sep 3 | 0/4,343 | 0/12 |
| Sep 4–10 | 0/4,647 | 0/46 |
| Sep 11–17 | 1/8,124 | 0/69 |
| Sep 18–24 | 0/7,288 | 1/206 |
| Sep 25–Oct 1 | 0/7,962 | 0/177 |
| Oct 2–8 | 0/7,603 | 0/37 |
| Oct 9–15 | 0/4,137 | 0/14 |
| Oct 16–22 | 0/6,459 | 0/25 |
| Oct 23–29 | 0/6,119 | 0/10 |
| Subtotals | 1/56,682 | 1/596 |
| Grand totals | 63/67,570 | 1/657 |

* Aerial ULV spraying of Dallas city and county with malathion was completed on August 27.

infection rate of 1 in every 167 tested. Over 57,000 mosquitoes were collected in the post-spray period, from day 2 until the end of the study on October 29; these yielded only two isolations of SLE virus. Both of these isolations were from mosquitoes collected about 3 weeks after spraying. They show that although SLE virus activity was greatly reduced, it was not entirely eliminated. It is obvious, however, that the

vector infection rate had become so drastically low after the spraying that large-scale transmission of the virus was highly unlikely.

*Effect of aerial spray on the human epidemic.* The human epidemic declined during the 2 to 3 weeks after the spraying. When the epidemic curve is presented by date of onset in relation to the date each area of residence was sprayed (figure 5), a mild decline in the number of reported human cases is seen beginning approximately 6 days after spraying. However, some decline in the number of cases could be seen before the spraying, and some cases occurred for up to 4 weeks after spraying. Three patients with confirmed cases, for example, had onset of illness 23 to 27 days after their respective areas of residence were sprayed.

TABLE 10

*Isolations of St. Louis encephalitis virus from* C. quinquefasciatus *listed in relation to time of ULV spraying of sampling areas, Dallas, Texas, August 10–October 29, 1966**

| No. days pre- or post-aero-spray | No. SLE virus isolations/No. *C. quinquefasciatus* tested | Infection rates | |
|---|---|---|---|
| Pre | | | |
| 8–14 | 2/240 | 1:120 | 1:167 (62:10,371) |
| 1–7 | 55/9,264 | 1:168 | |
| 0–1† | 5/867 | 1:173 | |
| Post | | | |
| 2–7 | 0/623 | <1:623 | 1:57,199 |
| 8–14 | 0/5,739 | <1:5,739 | |
| 15–21 | 0/5,221 | <1:5,221 | |
| 22–28 | 1/8,826‡ | 1:8,826 | |
| 29–67 | 0/36,790 | <1:36,790 | |

* Seven days of aerial spraying were carried out between August 19–27.

† Infected mosquitoes collected 0 to 1 day post-spray are included in the pre-spray infection rate calculations because they were either collected before the spray had lethal effect or before they had time to disperse from their protected shelters.

‡ One isolation of SLE virus was also made from 206 *C. tarsalis* collected during this same post-spray time period.

## DISCUSSION

In the years since outbreaks of SLE were first described in the early 1930's (1, 2), urban epidemics have occurred sporadically, primarily in the southern and central states (10, 12–14), but recently as far east and north as New Jersey (15). The largest in recent years have been those in the Tampa Bay area of Florida in 1962 (14) and Houston, Texas, in 1964 (10). In Texas in 1966 both Dallas and Corpus Christi had outbreaks of this disease but with somewhat different epidemiologic patterns (8, 16).

Despite increasing knowledge of the ecology of SLE, a reliable means of predicting the time or geographic locations of urban epidemics has not yet been developed. In Dallas, however, the unusual climatic conditions in the spring of 1966 appear to have contributed greatly to the breeding of the mosquito vectors required to sustain an

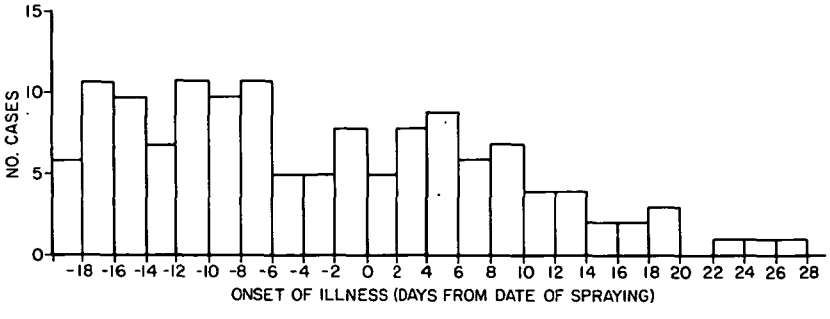


FIGURE 5. St. Louis encephalitis, Dallas County, 1966. Onset of illness relative to date area of residence was sprayed.

avian epizootic and the subsequent human epidemic. Extensive flooding, resulting in pools of stagnant water potentially rich in organic waste, occurred in many low-lying parts in the city. The municipal sewage treatment plant was within the flooded area and contributed to the general pollution. Proximity of these likely mosquito breeding sites to the lower socioeconomic areas of town, especially in the central and southern parts of the city, probably influenced the geographic distribution of cases.

Any epidemiologic consideration of a large urban epidemic of SLE must include the relative effects of race, socioeconomic status, and geographic location on the distribution of cases. Although there must be infective mosquitoes in an area before human cases can occur, socioeconomic and cultural factors may well affect the degree of human exposure to these disease-carrying vectors. For example, few of the homes in the lower socioeconomic areas of Dallas had airconditioning and window screening was often in poor repair. The inhabitants slept with windows open and thus were more likely to be bitten by the vector mosquitoes. It is also possible that even with equivalent exposures, differences in the attack rate by race may occur. However, in Houston in 1964, geographic location appeared to play the largest role, with cases occurring at a higher rate in central zones of the city and decreasing toward the periphery (10). Within each of the circumferential geographic areas considered, the attack rates by race were remarkably similar.

In Dallas an analysis similar to that in Houston, with additional consideration of large geographic regions of the city, suggested that all three variables were related to the distribution of the cases. Since these were probably interdependent, the extent to which each contributed to the distribution of cases could not be determined from the data available, particularly since recent changes in population distribution within the city appear to have been of such magnitude as to make assessment of differential attack rates by race or socioeconomic status in any geographic area unreliable.

The observed age distribution of cases is characteristic of illness related to SLE virus infection and is unique among the epidemic encephalitides known on this continent. A subsequent survey of family contacts of known patients in Dallas demonstrated that although the attack rate of clinical disease increased with age, the incidence of SLE antibodies was constant for all age groups sampled (17). This finding suggests that differences in infection rates are not responsible for the distribution of clinical illness by age, and that the more frequent manifestation of disease in the older age groups is more likely related to lesser host resistance. This impression is substantiated by the fact that the younger patients had symptoms of encephalitis less often than the older patients (table 3).

It should be recognized that the clinical categories defined in this study are arbitrary. More detailed clinical studies are presented elsewhere (18), and our categories are useful only as a rough gauge of the severity of illness. In our classification, however, the seven cases with confirmed recent SLE infections but no CNS symptoms (table 3, "other" column) appear somewhat unusual and may represent the coincidental discovery of subclinical SLE infection in the course of an unrelated illness. Serologic survey and interview of contacts of known cases during the epidemic showed no relationship between any recent symptoms and presumptively elevated titers of SLE neutralizing antibodies (17). However, historical inaccuracy, both in this survey and potentially among these seven cases under discussion, does not allow us to exclude the possibility that SLE virus infection sometimes manifests itself in organ systems other than the CNS.

In any case, we have arbitrarily included these seven cases in our epidemiologic description, despite the lack of clinical "encephalitis."

In this epidemic, ULV malathion was used for the first time to control an urban outbreak of SLE. Analysis of the effect of aerial spraying on the human epidemic must consider the length of the incubation period in humans, which has previously been estimated to be between 5 and 15 days (2). Although three cases in Dallas occurred more than 21 days after their area of residence was sprayed (figure 5), somewhat beyond the usually cited maximum incubation period, it cannot be concluded that the spraying was ineffective. These persons could have been exposed in parts of town which were sprayed later in the epidemic, or the incubation period of SLE might occasionally be longer than previously supposed.

It appears to be impossible to accurately evaluate the efficacy of the aerial spraying from a study of human cases alone. Although the number of human cases promptly declined after the spraying, the peak of the epidemic may already have occurred by the time spraying was instituted. It is clear, however, that after the aerial spraying with malathion a marked fall occurred in the number of mosquito vectors and in their infection rate. Therefore, one can logically assume that this treatment effectively reduced vector transmission. It is equally clear also that for any technique of vector control to actually prevent an epidemic, rather than just reduce the total number of cases, the potential epidemic must be recognized even earlier than it was in Dallas and the control methods applied even more promptly. Using only human surveillance, recognition any earlier than that in Dallas is unlikely. Further studies are needed to elucidate the factors which influence buildup of SLE virus in vectors and wild hosts and its spread to the human population. Perhaps a thorough evaluation of climatologic factors as they affect mosquito production (19) and an early summer surveillance of urban birds and mosquitoes for evidence of excessive virus activity (20) may provide the warning needed to exercise the most timely control.

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# Human Exposure to Mosquito-Control Pesticides — Mississippi, North Carolina, and Virginia, 2002 and 2003

Public health officials weigh the risk for mosquito-borne diseases against the risk for human exposure to pesticides sprayed to control mosquitoes (*1*). Response to outbreaks of mosquito-borne diseases has focused on vector control through habitat reduction and application of pesticides that kill mosquito larvae. However, in certain situations, public health officials control adult mosquito populations by spraying ultra-low volume (ULV) (<3 fluid ounces per acre [oz/acre]) mosquito-control (MC) pesticides, such as naled, permethrin, and d-phenothrin. These ULV applications generate aerosols of fine droplets of pesticides that stay aloft and kill mosquitoes on contact while minimizing the risk for exposure to persons, wildlife, and the environment (*2*). This report summarizes the results of studies in Mississippi, North Carolina, and Virginia that assessed human exposure to ULV naled, permethrin, and d-phenothrin used in emergency, large-scale MC activities. The findings indicated ULV application in MC activities did not result in substantial pesticide exposure to humans; however, public health interventions should focus on the reduction of home and workplace exposure to pesticides.

**FIGURE. Ultra-low volume, truck-mounted spraying for mosquito control — Mississippi, 2002**

Photo/CDC

## Mississippi, 2002

The 2002 West Nile virus (WNV) epidemic in Mississippi prompted an increase in MC activities, including application of ULV permethrin by truck-mounted foggers (Figure). Because of concerns about potential health effects from pesticides, the Mississippi Department of Health and CDC assessed whether MC activities increased individual urine pesticide metabolite concentrations. During September 8–19, 2002, investigators selected a geographically-random sample of 125 persons by using maps of two regions where public health officials applied MC pesticides and 67 persons from

**INSIDE**



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two control regions. Each participant completed a questionnaire describing home and occupational use of pesticides and provided a spot urine sample for analysis of pesticide metabolites 1–4 days after MC (i.e., within 5 half-lives). By using a cross-sectional design, investigators compared urine pesticide metabolite concentrations of exposed and unexposed study participants. Exposure to permethrin was verified by cross-referencing the global positioning systems location of participants with local MC spray routes. Permethrin was applied in MC regions at a concentration of 0.032 oz/acre.

Urine samples were analyzed at CDC by using tandem mass spectrometry (*3*). Urinary metabolite concentrations of 3-phenoxybenzoic acid (3pba), a metabolite of synthetic pyrethroid pesticides such as permethrin, did not differ significantly between MC and non-MC regions (geometric mean [GM] = 1.25 $\mu$g/L versus 1.13 $\mu$g/L, respectively). Although 3pba concentrations did not differ between participants who used pesticides at home or at work and those who did not, participants who used pesticides on pets (n = 17) had significantly higher (p = 0.02) mean 3pba concentrations than those who did not (n = 174) (4.27 $\mu$g/L versus 1.07 $\mu$g/L, respectively). These findings indicated that local MC activities did not lead to increased pesticide metabolite concentrations in the urine of participants.

## North Carolina, 2003

Hurricane Isabel made landfall in North Carolina on September 18, 2003. Because of ensuing rains and flooding, mosquito populations were expected to surge. To control mosquitoes and prevent transmission of WNV and other arboviruses, the North Carolina Department of Environmental and Natural Resources (NCDENR) sprayed ULV naled and permethrin.

The North Carolina Department of Health and Human Services, NCDENR, and CDC conducted a prospective exposure assessment of ULV spraying of pesticides. Investigators recruited 90 persons from a random sample of census blocks (that accounted for the population density) marked for spraying. Participants then completed a pre-spray questionnaire about household and occupational exposure to pesticides and provided urine samples to quantify concentrations of pesticide metabolites. On September 30, aircraft in North Carolina sprayed ULV naled at 0.7 oz/acre. In addition, trucks sprayed ULV permethrin (Biomist 30+30®) at 0.0014 lbs/acre. Eighteen hours after aerial spraying (approximately one half-life), each participant completed a post-spray questionnaire about household and occupational exposure to pesticides and provided a second urine sample. Urine samples were analyzed at CDC by using tandem mass spectrometry (*3*).

Of the 90 persons recruited to participate in this exposure assessment, 75 (83%) provided pre-spray and post-spray questionnaires and urine samples. The concentrations of all pre- and post-spray pesticide metabolites measured in participant urine samples were low (Table). Dimethylphosphate (DMP), a metabolite of organophosphate pesticides such as naled, was detected in 46% of pre-spray and 49% of post-spray urine samples (limit of detection [LOD] = 0.5 μg/L). The GM 3pba concentration from post-spray urine sampled was 0.2 μg/L. Generalized estimating equations (GEE) indicated no statistically significant differences in the urine concentrations of naled and permethrin metabolites before and after spraying. Participants who ate fresh fruits or vegetables ≤3 days before completing the pre-spray (n = 58) or post-spray (n = 37) questionnaires had significantly higher urine concentrations of dimethylthiophosphate than participants who did not pre-spray (n = 16) or post-spray (n = 37) (pre-spray: 3.2 μg/L versus 1.4 μg/L; GEE p = 0.02) (post-spray: 3.3 μg/L versus 1.2 μg/L; GEE p = 0.01). Two participants who worked on farms and/or handled pesticides had significantly higher urine concentrations of nonspecific organophosphorus pesticide metabolites (e.g., dimethyldithiophosphate, diethylthiophosphate, and diethylphosphate) than participants who did not work on farms (n = 73) or handle pesticides (n = 72).

## Virginia, 2003

To control mosquitoes and prevent transmission of arboviruses after Hurricane Isabel, the Virginia Department of Health (VDH) decided to spray ULV naled and d-phenothrin. VDH and CDC assessed exposure to ULV spraying of pesticides by randomly selecting 95 residents of high population-density census blocks marked for spraying. Participants then completed pre-spray questionnaires about household and occupational exposure to pesticides and provided urine samples to quantify concentrations of pesticide metabolites.

On September 30, aircraft sprayed ULV naled at 0.5 oz/acre while trucks sprayed ULV of d-phenothrin (Anvil 10+10®) at 0.0036 lbs/acre. Eighteen hours after spraying (approximately one half-life), each participant completed a post-spray questionnaire about household and occupational exposure to pesticides and provided a second urine sample. Urine samples were analyzed at CDC by using tandem mass spectrometry (*3*).

Of the 95 persons recruited for the assessment, 83 (87%) provided pre-spray and post-spray exposure questionnaires and urine samples. The concentrations of all pesticide metabolites measured in participants' urine samples were low (Table). DMP was detected in 42% of pre-spray and 48% of post-spray urine samples (LOD = 0.5 μg/L). The geometric mean 3pba concentration from post-spray urine samples was 0.6 μg/L. GEEs indicated no overall difference in the urine concentrations of naled and d-phenothrin metabolites before and after spraying.

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**Editorial Note:** Although ULV applications of naled and synthetic pyrethroids have a low toxicity to humans, occupational

**TABLE. Pre-spray and post-spray geometric mean concentrations (μg/L) of urine pesticide metabolites — North Carolina and Virginia, 2002 and 2003**

| Metabolite | North Carolina (n = 75) | | Virginia (n = 83) | | 95th percentile |
|---|---|---|---|---|---|
| | Pre-spray | Post-spray | Pre-spray | Post-spray | |
| Dimethylphosphate* | † | † | † | † | 13.0 |
| Dimethylthiophosphate§ | 2.7 | 1.9 | 2.5 | 2.0 | 46.0 |
| Dimethyldithiophosphate§ | 0.6 | 0.9 | 0.7 | 0.8 | 19.0 |
| Diethylphosphate§ | 0.6 | 1.3 | 0.8 | 1.6 | 13.0 |
| Diethylthiophosphate§ | 1.6 | 0.5 | 1.7 | 0.5 | 2.2 |
| Diethyldithiophosphate§ | † | † | † | † | 0.9 |
| 3-Phenoxybenzoic acid¶ | † | 0.2 | 0.3 | 0.6 | 3.4 |
| 4-Fluoro-3-phenoxybenzoic acid | † | † | † | † | 0.3 |
| *cis*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid** | † | † | † | † | 0.5 |
| *trans*-3-(2,2-dichlorovinyl) 2,2-dimethylcyclopropanecarboxylic acid** | 0.5 | 0.5 | 0.5 | 0.7 | 1.4 |
| *cis*-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylic acid** | † | † | † | † | 0.3 |

* Nonspecific metabolite of naled and other organophosphate pesticides.
† Metabolite concentrations were quantitated in <50% of samples.
§ Nonspecific metabolite of organophosphate pesticides (excluding naled).
¶ Nonspecific metabolite of permethrin/d-phenothrin and other synthetic pyrethroid pesticides.
** Nonspecific metabolite of synthetic pyrethroid pesticides (excluding permethrin/d-phenothrin).

studies suggest that excessive exposure to these pesticides can cause serious health effects (*4*). Prolonged exposure to high concentrations of naled and synthetic pyrethroids can cause dermatitis, reactive airway disease, gastrointestinal distress, central nervous system depression, paralysis, and death (*5*). Exposure often results from use of these pesticides in food production, treatment of wool, wood products, and pest-control efforts; however, few studies have quantitated the level of human exposure to MC pesticides in nonoccupational settings (*6*).

The studies described in this report represent the first efforts to quantitate human exposure to MC pesticides during large-scale MC activities. Two of these studies used a prospective crossover design that compared urine metabolite concentrations after ULV spraying of pesticides with baseline concentrations. Use of sensitive analytic methods in these studies indicated that the urine pesticide metabolite concentrations measured were low (parts per billion). The concentration of urine metabolites in these studies are comparable with those measured in the general population (*6,7*). In addition, these three studies did not indicate an overall increase of pesticide metabolite concentrations in the urine of participants after spraying during MC activities. The concentrations of naled, permethrin, and d-phenothrin during emergency ULV applications might be too low to cause important human exposure.

In certain participants, investigators found an association between home and/or work application of pesticides and pesticide metabolite concentrations. The concentrations in participants who had histories of exposure were within the range of the general U.S. population (*8*). These findings are consistent with occupational studies in which prolonged exposure to pesticides through several hours of work in plant nurseries and greenhouses was associated with low but measurable concentrations of urine pesticide metabolites (*9*). These findings also are compatible with a prospective study that quantitated higher 3pba concentrations in the urine of pest-control operators 1 day after spraying pyrethroids (*10*).

The findings in this report are subject to at least three limitations. First, although naled, permethrin, and d-phenothrin remain in the environment for a short period (e.g., naled has a 1-day half-life), CDC did not conduct environmental sampling to confirm the presence of pesticide on the ground after spraying. Second, the study did not quantify the effects of synergists such as piperonyl butoxide in Anvil 10+10®, which help increase the efficacy of synthetic pyrethroids. Finally, the use of self-reported questionnaire data limits the ability to quantify actual home or occupational pesticide exposure.

Aerial spraying with ULV naled and truck-mounted spraying with permethrin/d-phenothrin were not associated with an increase in urine pesticide metabolite concentrations among residents of these rural, suburban, and urban communities. These findings suggest that ULV application of naled, permethrin, and d-phenothrin is safe to humans as part of integrated vector control. The findings are noteworthy because ULV applications of pesticides that kill adult mosquitoes are an important tool in the public health response to WNV. Future studies should address the long-term safety of low-concentration exposure to naled and synthetic pyrethroid applications. In addition, public health interventions might be needed to reduce home and workplace exposure to pesticides.

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# Unintentional Topical Lindane Ingestions — United States, 1998–2003

Lindane* is an organochlorine pesticide found in certain prescription-only shampoos and topical lotions used to treat pediculosis (i.e., lice infestation) and scabies; lindane has been associated with human neurologic toxicity (*1,2*). In 2004, CDC was alerted to cases of illness caused by unintentional ingestion of lindane by persons mistaking the product for a liquid oral medication (e.g., cough syrup). To assess the extent of illness from ingestion of lindane, CDC, with assistance from the U.S. Environmental Protection Agency, Food and Drug Administration (FDA), and state health departments, collected case reports and analyzed data from the Sentinel Event Notification System for Occupational Risks-Pesticides (SENSOR-Pesticides) program and the Toxic Exposure Surveillance System (TESS). This report summarizes the results of that analysis, which identified 870 cases of unintentional lindane ingestion during 1998–2003, and describes two examples of lindane ingestions. To reduce the risk of lindane ingestion, public health authorities should alert clinicians to the hazards of lindane and the importance of following FDA usage guidelines, which include dispensing lindane in manufacturer-produced, 1- or 2-ounce single-use containers.

## Case Reports

**Case 1.** In November 2004, the Washington State Department of Health reported that a boy aged 3 years ingested approximately 1 teaspoon of 1% lindane shampoo from a previously used 2-ounce bottle. Subsequently, the mother induced vomiting in the boy twice; 1 hour later the boy collapsed and experienced a tonic-clonic seizure lasting 4–5 minutes. After 3 hours, the child was discharged from the emergency department in stable condition.

**Case 2.** In December 2003, a man aged 47 years in Texas mistakenly ingested 1 ounce of lindane (percentage concentration unknown) from a bottle he believed to be cough syrup. The man vomited; he contacted the poison control center the following morning. He did not seek clinical evaluation.

## Surveillance Data

Data were analyzed from pesticide poisoning surveillance systems participating in the SENSOR-Pesticides program† to identify symptomatic cases involving unintentional topical lindane ingestions during 1998–2003. Cases were classified as definite, probable, possible, or suspicious based on the clinical interpretation of signs or symptoms reported by a physician or patient, and evidence of lindane ingestion (*3,4*). Cases were also obtained from TESS§, which is maintained by the American Association of Poison Control Centers; poison information specialists determined which cases had signs and symptoms consistent with lindane exposure. Illness severity was categorized for all cases. Excluded were cases involving ingestion of veterinary and agricultural pesticide products that contained lindane.

During 1998–2003, TESS reported 857 symptomatic cases of unintentional lindane ingestion (Figure); none of the cases were reported as resulting in death. Severity was low in 778 cases (91%), moderate in 71 cases (8%), and high in eight cases (1%) (*4*). Among 823 patients with known ages, median age was 13 years (range: <1–86 years); 53% were female. Signs and symptoms included vomiting (59%), nausea (18%), oral irritation (19%), abdominal cramping (4%), cough (4%), and seizure (3%).

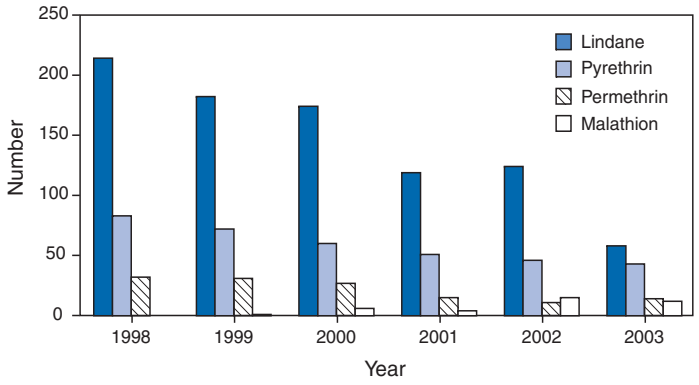
During 1998–2003, SENSOR-Pesticides identified a total of 13 symptomatic cases of unintentional lindane ingestion. Four cases (31%) were classified as definite, two (15%) as probable, six (46%) as possible, and one (8%) as suspicious. Severity was low in eight cases (62%), moderate in three cases (23%), and high in two cases (15%) (*3*). Median age was 7 years (range: <1–58 years), and 69% were male. Signs and symptoms included vomiting (69%), nausea (46%), headache (23%), seizure (23%), abdominal cramping (8%), and confusion (8%). Six (46%) cases in children and four (31%) cases

*Lindane is also referred to as gamma-hexachlorocyclohexane.

†SENSOR-Pesticides is a surveillance program coordinated by the National Institute for Occupational Safety and Health (NIOSH) at CDC and conducted by health departments in nine states. Most participating states collect information on both nonoccupational and occupational pesticide poisonings from various sources (e.g., poison control centers, workers' compensation agencies, or state departments of agriculture). However, priority is given to occupational cases; therefore, the number of nonoccupational poisoning cases is limited.

§TESS receives reports from nearly all poison control centers nationwide.

**FIGURE. Number of symptomatic cases from unintentional ingestion of medication for pediculosis and scabies, by medication and year of exposure — Toxic Exposure Surveillance System and the Sentinel Event Notification System for Occupational Risks-Pesticides program, 1998–2003.**



in adults were the result of mistaking lindane for cough syrup; two (15%) cases were in unsupervised children who drank lindane, and one (8%) case was the result of pharmacy error (i.e., lindane was recovered from a bottle labeled albuterol).

In addition to lindane, FDA-approved treatments for pediculosis include two over-the-counter medications (pyrethrin/piperonyl butoxide and permethrin) and malathion, a prescription-only therapy. During 1998–2003, TESS identified 523 symptomatic cases of unintentional ingestion of these alternative medications (Figure). Median age was 9 years (range: <1–67 years). Among TESS reports, unintentional lindane ingestions were more likely to produce illness (857 illnesses of 1,463 ingestions [58%]) than unintentional ingestions of each of three other medications, and more likely to produce illness than all three of those medications combined (523 illnesses of 1,691 ingestions [31%]; odds ratio = 3.16, 95% confidence interval = 2.72–3.67).

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**Editorial Note:** Pediculosis and scabies are common human parasitic infestations. This report indicates that when lindane, a treatment for pediculosis and scabies, is unintentionally ingested, illness can occur, including vomiting and seizures. In 1995, lindane was changed to a second-line therapy for pediculosis because safer alternatives existed (*5*). Lindane also had the slowest pediculicidal and least effective ovicidal activity compared with three other approved pediculicides (i.e., 1% permethrin, 0.3% pyrethrin, and 0.5% malathion) (*6*). In 2003, in light of continued postmarketing surveillance reports of toxicity, FDA revised product labeling guidelines to limit the amount of lindane dispensed to 1- or 2-ounce single-use containers and to require providing patients with a Medication Guide warning of risks from inappropriate use. In addition, FDA issued a Public Health Advisory with these changes (*7*). The new advisory, along with a substantial increase in retail price for lindane, appear to have resulted in a declining number of cases of lindane ingestion (Figure). This decline is similar to the 67% decrease in lindane prescriptions from 1998 to 2003 (*8*).

Before the advisory, bottles of bulk lindane were sometimes repackaged by pharmacies into smaller bottles resembling those used for liquid oral medications (e.g., cough syrup). This resemblance likely contributed to many unintentional ingestions. Subsequent to the advisory, bottles of bulk lindane still in use were not recalled from pharmacies. Therefore, some repackaging might still occur. In addition, consumers might have repackaged lindane in their homes.

In September 2004, the North American Task Force on Lindane drafted an action plan for future use. On January 1, 2005, Canada withdrew registration of lindane for agricultural pest control; Mexico is working on a plan to phase out all uses of lindane. However, with the exception of California, which banned lindane for medicinal use on January 1, 2002, U.S. representatives to the North American Commission for Environmental Cooperation announced that the United States will continue to allow use of lindane as both a pesticide and pharmaceutical (*9*).

The findings in this report are subject to at least three limitations. First, because of the passive surveillance methodology of TESS and SENSOR, the number of reported cases is likely fewer than the number of actual cases. Second, certain eligible cases might have been inadvertently excluded because of erroneous information that suggested exposure to lindane in a veterinary or agricultural product. Finally, although all cases were symptomatic, the possibility of false positives cannot be excluded. Because clinical findings of lindane poisoning are nonspecific and no standard diagnostic test exists, certain illnesses related temporally to lindane exposure might not have been caused by the exposure.

Lindane use in shampoos and lotions for treatment of pediculosis and scabies is declining. However, because of the toxicity of lindane and the potential for illness from unintentional ingestion, health-care providers should be educated regarding appropriate use and packaging. Lindane is a second-line therapy for both scabies and lice and should not be tried unless other treatments have failed or are intolerable; use of lindane also should be avoided for persons weighing less than 110 pounds (50 kg). Because of the risk for toxicity, treatment should not be repeated, even if itching persists; itching can occur, even after successful treatment (especially for scabies) and can be treated symptomatically. In addition, pharmacists should not transfer lindane to other containers and should only dispense lindane in manufacturer-provided 1- or 2-ounce containers. Finally, periodic educational outreach programs can help increase awareness among health-care providers of the new lindane use guidelines.

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## Surveillance for Laboratory-Confirmed, Influenza-Associated Hospitalizations — Colorado, 2004–05 Influenza Season

The number of annual hospitalizations for influenza and pneumonia associated with influenza viruses in the United States is estimated at 95,000 (*1*); however, no state-based or national surveillance system exists to monitor these events in all age groups, and population-based numbers of laboratory-confirmed, influenza hospitalizations are unknown. Certain existing surveillance systems provide population-based national estimates of influenza-related hospitalizations based on sampling methodology (i.e., the National Hospital Discharge Survey) or sentinel surveillance; however, these systems are not timely, population-based for all ages, and available at the state level. The Emerging Infections Program (EIP) conducts population-based surveillance for laboratory-confirmed, influenza-related hospitalizations of persons aged <18 years in 11 metropolitan areas, and the New Vaccine Surveillance Network (NVSN) provides population-based estimates of laboratory-confirmed influenza hospitalization rates among children aged <5 years who were prospectively enrolled and tested for influenza in three sentinel counties. The U.S. Department of Health and Human Services recommends that states develop strategies to monitor influenza-related hospitalizations (*2*). This report describes a surveillance system for laboratory-confirmed, influenza-associated hospitalizations in all age groups in Colorado that was implemented for the 2004–05 influenza season. The findings indicate that implementation of statewide, population-based surveillance for influenza-associated hospitalizations is feasible and useful for assessing the age-specific burden of serious influenza-associated morbidity and the relative severity of influenza seasons.

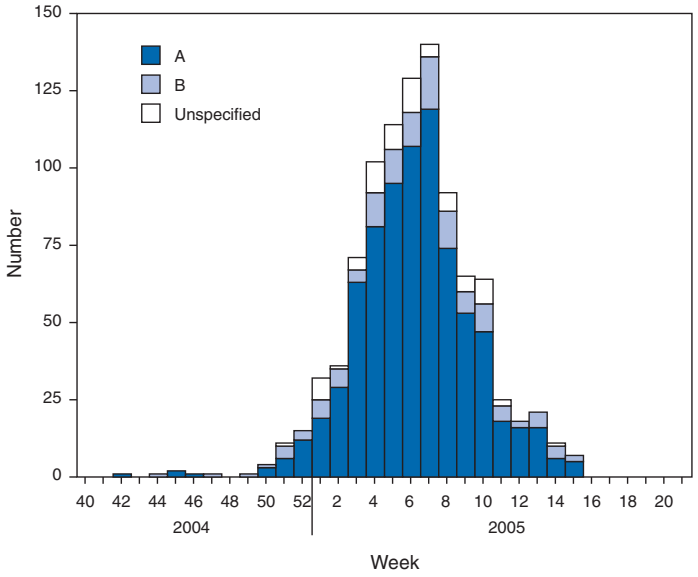
On September 30, 2004, influenza-ssociated hospitalizations became a condition reportable by Colorado health-care providers. An influenza-associated hospitalization was defined for surveillance purposes as a hospital admission accompanied by an appropriate laboratory test result for influenza, including results from rapid diagnostic tests. Population estimates for 2003 (overall 4.6 million) by age group were obtained from the Colorado Department of Local Affairs and used to compute annual age-specific rates of influenza-associated hospitalization. Case reports of influenza-associated hospitalization contained the same core variables that are collected for all reportable diseases in Colorado, including patient identifying, locating, and demographic information; name of reporting agency; physician name and contact information; specimen collection date, specimen type, and test type; test result and date, and report date,

Reporting of notifiable diseases by 68 hospitals in Colorado is performed primarily by infection-control practitioners (ICPs). Many ICPs enter data directly into the state's web-based disease reporting system; however, others fax reports to the Colorado Department of Public Health and Environment (CDPHE) or report directly to local health departments. During the 2004–05 influenza season, ICPs ascertained cases of influenza-associated hospitalization by reviewing clinical laboratory and admission information routinely available to them. ICPs entered 74% of reported influenza-associated hospitalizations directly into the state's reporting system; state or local health department staff members entered the remaining 26%.

Since the 1999–00 influenza season in Colorado, influenza surveillance data have been compiled weekly from multiple sources (e.g., influenza-like illness [ILI] reported by sentinel providers and one health maintenance organization; outbreaks of influenza in nursing homes; absenteeism reported by sentinel schools; and influenza virus typing and subtyping data from state and clinical laboratories) and disseminated via an electronic summary to local health departments. However, none of these influenza surveillance methods are population-based, and none focus on hospitalization.

As of April 16, 2005, a total of 964 influenza-associated hospitalizations had been reported by 50 hospitals, producing a rate of 21.0 per 100,000 persons during the 2004–05 influenza season. Reported cases peaked during the week ending February 19, 2005 (Figure), which was also the peak week for the percentage of patient visits for ILI reported by sentinel health-care providers in Colorado (CDPHE, unpublished data, 2005). Influenza virus type–specific testing results were available for 896 (92.9%) reported cases, of which 86.3% were influenza A and 13.7% were influenza B. The most frequently

**FIGURE. Number* of laboratory-confirmed, influenza-associated hospitalizations reported† by 50 hospitals, by influenza virus type and week of diagnosis — Colorado, 2004–05 influenza season**




* N = 964.
† As of April 16, 2005 (week 15).

reported test type was rapid influenza testing (88.0%), followed by direct fluorescent antibody (5.8%) and viral culture (5.6%). The highest influenza-associated hospitalization rates were in persons aged ≥80 years (207.3 per 100,000 population) and children aged <6 months (183.0 per 100,000), followed by persons aged 70–79 years (78.0 per 100,000) and children aged 6–23 months (66.3 per 100,000) (Table). Persons aged ≥60 years accounted for 51.4% of reported cases. The median time from specimen collection to disease report was 2 days, with 86% of cases reported within 7 days.

**TABLE . Number, percentage, and rate* of laboratory-confirmed, influenza-associated hospitalizations reported† by 50 hospitals, by age group — Colorado, 2004–05 influenza season**

| Age group | No. | (%) | Rate |
|---|---|---|---|
| <6 mos | 63 | (6.5) | 183.0 |
| 6–23 mos | 68 | (7.1) | 66.3 |
| 2–4 years | 56 | (5.8) | 28.9 |
| 5–17 years | 51 | (5.3) | 6.1 |
| 18–39 years | 87 | (9.0) | 5.8 |
| 40–49 years | 51 | (5.3) | 6.8 |
| 50–59 years | 92 | (9.5) | 16.4 |
| 60–69 years | 101 | (10.5) | 33.5 |
| 70–79 years | 157 | (16.3) | 78.0 |
| ≥80 years | 238 | (24.7) | 207.3 |
| **Total** | **964** | **(100)** | **21.0** |

* Per 100,000 population.
† As of April 16, 2005 (week 15).

**Reported by:** *K Gershman, MD, Colorado Dept of Public Health and Environment.*

**Editorial Note:** Previous efforts to determine the impact of influenza on hospitalizations were based on statistical modeling methods (e.g., using national hospital discharge survey data) (*1,3–6*). The overall rate of influenza-associated hospitalizations (21.0 per 100,000 population) reported in Colorado during the 2004–05 influenza season through the new statewide notifiable disease surveillance is similar to published estimates based on national hospital discharge data. These estimates include a mean of 36.8 per 100,000 population (range: 7.8–71.4) for primary listed pneumonia and influenza hospitalizations for influenza seasons 1979–80 through 2000–01 (*1*) and a mean of 49 per 100,000 population (range: 8–102) for excess pneumonia and influenza hospitalizations for influenza seasons 1969–70 through 1994–95 (*3*). Estimates based on hospital discharge data are not available nationally for at least 12 months and on the state level for several months; however, statewide surveillance for influenza-associated hospitalizations in Colorado provided real-time, population-based incidence of influenza-associated hospitalization. Surveillance also confirmed the high risk for hospitalization among the youngest and oldest populations.

The findings in this report are subject to at least four limitations. First, influenza testing is not likely to be performed on all persons hospitalized with acute respiratory illness or with exacerbations of chronic respiratory or cardiovascular disease resulting from influenza infection. Therefore, surveillance for hospitalizations based on positive influenza testing underestimates the number of influenza-associated hospitalizations. Second, the sensitivity of rapid influenza tests is lower than that of viral culture and varies by test (*7*), which also contributes to underestimates of influenza-related illness. Third, rapid influenza tests can have low positive predictive value both early and late in the influenza season, when the prevalence of circulating influenza viruses is low (*7*). Finally, the data in this report are from one influenza season; the incidence of influenza-associated hospitalization and possibly the resources needed to conduct surveillance will vary depending on the severity of the influenza season.

CDC maintains and coordinates a national influenza surveillance system that allows public health officials to know when and where influenza activity is occurring, determine what types of influenza viruses are circulating, detect changes in the influenza viruses, track influenza-related illness, and measure the impact of influenza on overall mortality in the United States (*8*). However, none of these national components provide population-based influenza-related hospitalization rates for all age groups.

Surveillance for influenza-associated hospitalizations can provide multiple benefits to Colorado and other states that might adopt similar systems. The system provides improved ability to assess the severity of influenza seasons, track the time course of the season, determine which populations are most affected by severe influenza-related illness, and focus prevention and control efforts on those populations.

A national surveillance system similar to the one implemented in Colorado could provide data to 1) monitor and describe the incidence, distribution, and basic epidemiologic characteristics of hospitalizations related to influenza virus infection; 2) guide future influenza immunization policy (e.g., expansion of immunization recommendations for children); 3) rapidly recognize influenza seasons in which the number of hospitalizations appears unusually high; and 4) help identify an influenza pandemic and direct public health response. The recent development and widespread use of rapid influenza testing makes it feasible and desirable to use case reporting based on positive laboratory testing to monitor influenza-associated hospitalizations.

**Acknowledgments**

The findings in this report are based, in part, on contributions by M Evdemon-Hogan, MSPH, B Stone, MSPH, Colorado Dept of Public Health and Environment. A Postema, MPH, L Brammer, MPH, T Uyeki, MD, Influenza Br, National Center for Infectious Diseases, CDC.

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# Lymphocytic Choriomeningitis Virus Infection in Organ Transplant Recipients — Massachusetts, Rhode Island, 2005

*On May 26, this report was posted as an* MMWR Dispatch *on the* MMWR *website* (http://www.cdc.gov/mmwr).

On May 3, 2005, CDC received a report of severe illness in four patients who had received solid organ transplants from a common donor. All four organ recipients subsequently were found to have evidence of infection with lymphocytic choriomeningitis virus (LCMV), a rodent-borne Old World arenavirus. Preliminary findings from the ensuing investigation indicate the source of infection likely was an infected hamster in the donor's home. This report summarizes the ongoing investigation and provides information on exposure risks and possible prevention measures.

In early April, in Rhode Island, a woman with a medical history remarkable only for hypertension and 1 week of headache had sudden onset of hemiplegia caused by a stroke, followed by brainstem herniation and brain death within 3 days. A thorough evaluation was not suggestive of infection.

Family members of the woman consented to donation; organs and tissues were recovered, including the liver, the lungs, both kidneys, both corneas, and skin. Within 3 weeks after transplantation, the four persons who received the liver, lungs, and two kidneys had abnormalities of liver function and blood coagulation, and dysfunction of the transplanted organ. Signs, symptoms, and clinical laboratory test results varied in these patients and included fever, localized rash, diarrhea, hyponatremia, thrombocytopenia, hypoxia, and kidney failure. Three of the four organ recipients died, 23–27 days after transplantation. The fourth patient, a kidney recipient, survived. Histopathologic findings varied in the four cases, but hepatocellular necrosis was common to all three decedents on autopsy. The two cornea recipients were asymptomatic. Skin was not transplanted.

When the cause of illness among the recipients was not identified through extensive diagnostic testing and suspicion of transplant-transmitted infection arose, tissue and blood samples from the donor and recipients were sent from the Rhode Island Department of Health and the Massachusetts Department of Public Health to CDC. LCMV was identified as the cause of illness in all four organ recipients; diagnosis was made in tissues from multiple organs through immunohistochemical staining, reverse transcriptase-polymerase chain reaction (RT-PCR), enzyme-linked immunosorbent assays (i.e., IgM capture and indirect IgG), and viral culture on Vero E6 cells. Sequencing of the virus genome confirmed its identity as LCMV. Based on the diagnosis of LCMV infection,

the surviving kidney transplant recipient was treated with intravenous ribavirin and reduction in his immunosuppressive drug regimen; the patient improved clinically.

## Epidemiologic Investigation

To determine the source of LCMV infection, investigations were conducted at the hospitals involved in organ recovery and transplantation and at the coordinating organ procurement organization. Interviews also were conducted at locations where the donor had spent substantial time in the month preceding her death.

Interviews with hospital and organ bank staff members revealed no likely sources of LCMV infection in the hospital or organ-recovery settings. Environmental assessment at locations the donor frequented (e.g., home and work) revealed limited opportunities for exposure to wild rodents; the sole location noted with rodent infestation was a garden shed at her home. Interviews with family members of the donor determined that a pet hamster had been acquired recently. The hamster was cared for primarily by another family member. No illnesses compatible with LCMV had been reported in the donor or family members during the month preceding the donor's death. Further investigation of the source of infection, including rodent traceback, is ongoing.

## Laboratory Investigation

Family members of the donor were tested for LCMV antibodies. The family member who cared for the hamster had specific IgM and IgG antibodies to LCMV. No other family member had detectable IgG or IgM antibodies to LCMV. All available donor tissues were tested, and no evidence of LCMV was determined by serology, immunohistochemistry, RT-PCR, or viral culture. However, the pet hamster was determined positive for LCMV by virus isolation, RT-PCR, and immunohistochemistry. Genetic sequencing to enable comparison of patient and rodent virus isolates is planned.

**Reported by:** *Rhode Island Hospital, Providence; Rhode Island Dept of Health. New England Organ Bank, Newton; Massachusetts General Hospital, Brigham and Women's Hospital, Boston; Massachusetts Dept of Public Health. Infectious Disease Pathology Activity, Special Pathogens Br, Div of Viral and Rickettsial Diseases, Div of Healthcare Quality Promotion, National Center for Infectious Diseases; EIS officers, CDC.*

**Editorial Note:** LCMV infection usually is either asymptomatic or causes mild self-limited illness in otherwise healthy persons. LCMV can cause aseptic meningitis, but the infection is rarely fatal (*1*). Infection during pregnancy can result in vertical transmission of the virus from mother to fetus; LCMV infection during the first or second trimesters can lead to severe illness in the fetus (*2*). Serologic studies conducted in urban areas of the United States have indicated that prevalence of LCMV infection among humans is approximately 5% (*3,4*). The house mouse (*Mus musculus*) is the primary reservoir for LCMV, with a prevalence of infection of 3%–40%; a high degree of focality often is noted (*3,5,6*). However, other types of rodents (e.g., hamsters or guinea pigs) can be infected after contact with infected house mice (*7*); these rodents also have been implicated in human infection. Animals can become ill or can be asymptomatic. Infection in humans occurs primarily through exposure to secretions or excretions of infected animals (*8*).

Human-to-human transmission of LCMV has not been reported, with the exception of vertical transmission from an infected mother to fetus (*2*). A large outbreak associated with pet hamsters sold by a single distributor was reported in 1975, when 181 symptomatic cases among persons with hamster contact were identified in 12 states; no deaths occurred (*9*). In 2003, a cluster of solid organ transplant-associated meningoencephalitis deaths in Wisconsin was investigated and determined to be associated with LCMV infection. In that investigation, testing of donor tissues did not reveal any evidence of infection (*10*), and no exposures to rodents were found. Acute LCMV infection in an organ donor is thought to be a rare event.

In the case described in this report, neither the donor nor the infected family member had illness characteristic of LCMV infection. In the organ recipients, transplantation of LCMV-infected organs in the setting of immunosuppression likely increased disease severity. Although most persons infected with LCMV do not exhibit symptoms and the risk for LCMV infection from pet rodents is considered low, persons (especially pregnant women) should be aware of the possible risks associated with LCMV infection. Persons can minimize risk of LCMV infection from pet rodents by being attentive to proper hand hygiene and environmental cleaning. Additional information on handling pet rodents is available at http://www.cdc.gov/healthypets/animals/pocket_pets.htm. Additional information on LCMV is available at http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/lcmv.htm.

Health-care providers should be aware that LCMV can be transmitted through organ transplantation. Any unexpected infectious syndromes in recipients after solid organ or tissue transplantation should trigger concern about the possibility of transplant-associated transmission of an infectious agent. Although such instances are rare, providers should alert the associated organ procurement organization, tissue bank, and public health authorities when such events are suspected. The lifesaving benefits from transplanted organs outweigh the potential risk for unidentified infectious diseases; opportunities to increase donation should be encouraged.

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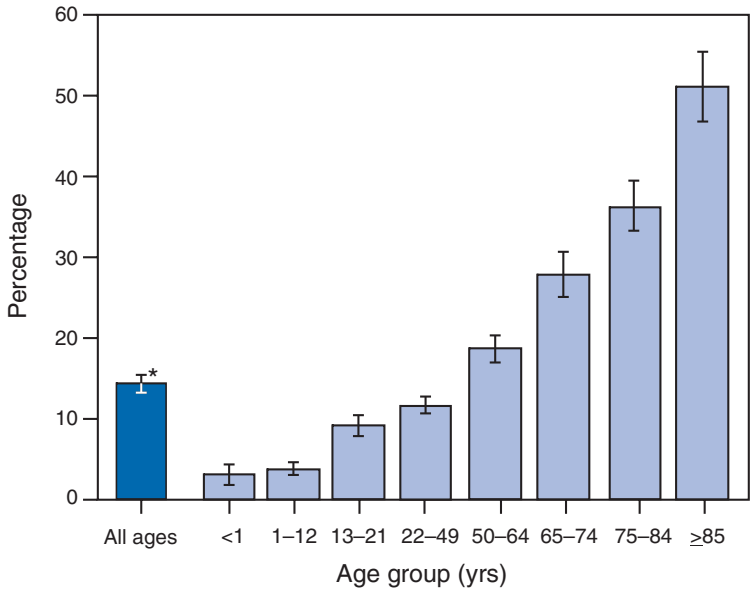
# QuickStats

**FROM THE NATIONAL CENTER FOR HEALTH STATISTICS**

## Patient Arrivals by Ambulance at Emergency Departments, by Age Group — United States, 2003




* 95% confidence interval.

Overall, arrivals by ambulance accounted for 14.2% (approximately 16 million) of visits to emergency departments (EDs) in 2003. The proportion arriving by ambulance increased with age. Approximately 50% of adults aged ≥85 years arrived at EDs by ambulance, compared with 4% of children aged ≤12 years.

**SOURCE:** 2003 National Hospital Ambulatory Medical Care Survey. Available at http://www.cdc.gov/nchs/data/ad/ad358.pdf.

*Notice to Readers*

## World Environment Day — June 5, 2005

"Green Cities" is the theme of World Environment Day, June 5, 2005. This annual event, established by the United Nations General Assembly in 1972, highlights environmental issues, encourages persons worldwide to participate in sustainable and equitable development, and promotes awareness of the importance of communities in changing attitudes toward environmental concerns. San Francisco is the host city for World Environment Day 2005.

When roads and buildings replace natural land cover, urban air temperatures can exceed those of the surrounding countryside by as much as 41°F (5°C) (*1*). Creation or preservation of green spaces in cities can mitigate this so-called heat-island effect. Green areas in urban settings also produce oxygen, absorb carbon dioxide, and enhance air quality; provide storm water control; and provide habitat for urban wildlife. Well-managed urban settlements can support growing urban populations by limiting their impact on the environment and improving their health. National and local policies can discourage waste, encourage conservation, and promote sustainable solutions.

Ongoing activities at CDC contribute to best practices for environmental public health nationally and internationally. CDC aims to protect all communities from environmental threats and to promote health in places where persons live, work, learn, and play. These activities include preventing lead poisoning, controlling asthma, reducing the health impact of natural and technological disasters, reducing exposure to toxic substances, preparing for emergencies involving radiation or radioactive materials, environmental public health tracking (*2*), and using laboratory testing to determine exposures to chemicals in the environment. CDC also provides information about environmental toxins and hazards (*3,4*). CDC's environmental health activities are detailed at http://www.atsdr.cdc.gov and http://www.cdc.gov/nceh. Additional information about World Environment Day 2005 is available at http://www.wed2005.org.

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*Notice to Readers*

## Assessment of the Distinctions Between Public Health Practice and Research

The Council of State and Territorial Epidemiologists (CSTE) has released a report, *Public Health Practice vs. Research: A Report for Public Health Practitioners Including Cases and Guidance for Making Distinctions*. This collaborative work of CSTE, Johns Hopkins Bloomberg School of Public Health, and Georgetown University Law Center may help public health officials, researchers, institutional review board (IRB) members, and their staffs distinguish between practice and research. Existing research, concepts, criteria, and cases are provided in the report to guide such distinctions. The CSTE report is available at http://www.cste.org/pdffiles/newpdffiles/cstephresrpthodgefinal.5.24.04.pdf.

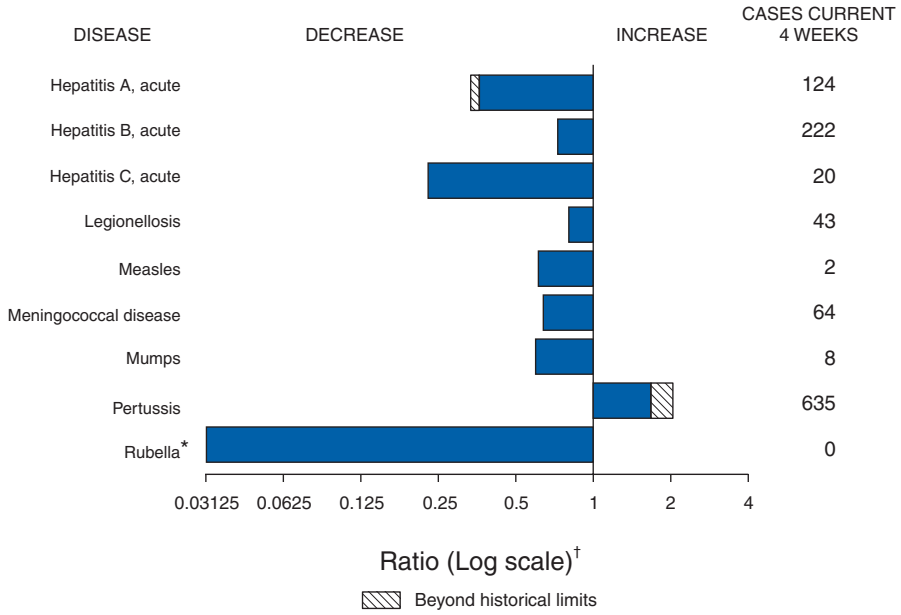
*Notice to Readers*

## New Edition of *Health Information for International Travel*

CDC announces the availability of the 2005–2006 edition of *Health Information for International Travel* (i.e., the Yellow Book). This edition, which has been completely revised, updated, and reorganized, now includes references listed at the end of each section.

Sections of the book have been expanded substantially, including those covering immunosuppressed travelers, disabled travelers, cruise-ship travel, and children who travel. New sections have been added on air travel, norovirus infection, SARS, and legionellosis. Copies can be ordered through the CDC Travelers' Health website at http://www.cdc.gov/travel.

**FIGURE I. Selected notifiable disease reports, United States, comparison of provisional 4-week totals May 28, 2005, with historical data**




* No rubella cases were reported for the current 4-week period yielding a ratio for week 21 of zero (0).
† Ratio of current 4-week total to mean of 15 4-week totals (from previous, comparable, and subsequent 4-week periods for the past 5 years). The point where the hatched area begins is based on the mean and two standard deviations of these 4-week totals.

**TABLE I. Summary of provisional cases of selected notifiable diseases, United States, cumulative, week ending May 28, 2005 (21st Week)***

| Disease | Cum. 2005 | Cum. 2004 | Disease | Cum. 2005 | Cum. 2004 |
|---|---|---|---|---|---|
| Anthrax | — | — | Hemolytic uremic syndrome, postdiarrheal† | 45 | 29 |
| Botulism: | | | HIV infection, pediatric†¶ | 116 | 155 |
| foodborne | 5 | 4 | Influenza-associated pediatric mortality†** | 34 | — |
| infant | 21 | 27 | Measles | 15†† | 14§§ |
| other (wound & unspecified) | 10 | 3 | Mumps | 101 | 87 |
| Brucellosis | 30 | 42 | Plague | 2 | — |
| Chancroid | 10 | 19 | Poliomyelitis, paralytic | — | — |
| Cholera | 1 | 4 | Psittacosis† | 8 | 4 |
| Cyclosporiasis† | 364 | 88 | Q fever† | 27 | 27 |
| Diphtheria | — | — | Rabies, human | 1 | — |
| Domestic arboviral diseases | | | Rubella | 4 | 8 |
| (neuroinvasive & non-neuroinvasive): | — | — | Rubella, congenital syndrome | 1 | — |
| California serogroup†§ | — | 4 | SARS†** | — | — |
| eastern equine†§ | — | — | Smallpox† | — | — |
| Powassan†§ | — | — | *Staphylococcus aureus*: | | |
| St. Louis†§ | — | 1 | Vancomycin-intermediate (VISA)† | — | — |
| western equine†§ | — | — | Vancomycin-resistant (VRSA)† | — | 1 |
| Ehrlichiosis: | — | — | Streptococcal toxic-shock syndrome† | 65 | 80 |
| human granulocytic (HGE)† | 33 | 50 | Tetanus | 5 | 5 |
| human monocytic (HME)† | 34 | 28 | Toxic-shock syndrome | 40 | 38 |
| human, other and unspecified † | 10 | 6 | Trichinellosis¶¶ | 5 | — |
| Hansen disease† | 16 | 45 | Tularemia† | 14 | 21 |
| Hantavirus pulmonary syndrome† | 5 | 4 | Yellow fever | — | — |

—: No reported cases.
* Incidence data for reporting years 2004 and 2005 are provisional and cumulative (year-to-date).
† Not notifiable in all states.
§ Updated weekly from reports to the Division of Vector-Borne Infectious Diseases, National Center for Infectious Diseases (ArboNet Surveillance).
¶ Updated monthly from reports to the Division of HIV/AIDS Prevention, National Center for HIV, STD, and TB Prevention. Last update April 24, 2005.
** Updated weekly from reports to the Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases.
†† Of 15 cases reported, nine were indigenous and six were imported from another country.
§§ Of 14 cases reported, five were indigenous and nine were imported from another country.
¶¶ Formerly Trichinosis.

**TABLE II. Provisional cases of selected notifiable diseases, United States, weeks ending May 28, 2005, and May 29, 2004 (21st Week)***

| Reporting area | AIDS | | Chlamydia† | | Coccidioidomycosis | | Cryptosporidiosis | |
|---|---|---|---|---|---|---|---|---|
| | Cum. 2005§ | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 |
| UNITED STATES | 13,232 | 16,816 | 344,968 | 368,769 | 1,625 | 1,832 | 724 | 968 |
| NEW ENGLAND | 532 | 566 | 11,239 | 12,166 | — | — | 38 | 57 |
| Maine | 4 | 5 | 864 | 783 | N | N | 3 | 9 |
| N.H. | 7 | 23 | 740 | 699 | — | — | 6 | 14 |
| Vt.¶ | 3 | 13 | 409 | 467 | — | — | 9 | 6 |
| Mass. | 275 | 151 | 5,862 | 5,381 | — | — | 14 | 20 |
| R.I. | 47 | 66 | 1,361 | 1,401 | — | — | 1 | 1 |
| Conn. | 196 | 308 | 2,003 | 3,435 | N | N | 5 | 7 |
| MID. ATLANTIC | 2,558 | 3,919 | 41,537 | 45,770 | — | — | 105 | 157 |
| Upstate N.Y. | 253 | 462 | 8,693 | 8,916 | N | N | 28 | 30 |
| N.Y. City | 1,476 | 2,145 | 13,269 | 14,097 | — | — | 24 | 50 |
| N.J. | 413 | 670 | 4,532 | 7,383 | N | N | 7 | 12 |
| Pa. | 416 | 642 | 15,043 | 15,374 | N | N | 46 | 65 |
| E.N. CENTRAL | 1,204 | 1,446 | 53,962 | 66,354 | 3 | 5 | 136 | 246 |
| Ohio | 185 | 233 | 14,443 | 16,961 | N | N | 50 | 53 |
| Ind. | 165 | 164 | 8,104 | 7,376 | N | N | 11 | 30 |
| Ill. | 661 | 703 | 14,836 | 19,033 | — | — | 2 | 41 |
| Mich. | 138 | 263 | 9,596 | 15,642 | 3 | 5 | 22 | 48 |
| Wis. | 55 | 83 | 6,983 | 7,342 | N | N | 51 | 74 |
| W.N. CENTRAL | 318 | 323 | 20,613 | 22,601 | 3 | 4 | 109 | 99 |
| Minn. | 88 | 79 | 3,117 | 4,666 | 3 | N | 33 | 39 |
| Iowa | 41 | 20 | 2,748 | 2,757 | N | N | 18 | 14 |
| Mo. | 132 | 127 | 9,123 | 8,371 | — | 3 | 42 | 18 |
| N. Dak. | 5 | 14 | 412 | 785 | N | N | — | — |
| S. Dak. | 9 | 5 | 1,142 | 1,019 | — | — | 7 | 11 |
| Nebr.¶ | 5 | 21 | 1,498 | 2,114 | — | 1 | 1 | 5 |
| Kans. | 38 | 57 | 2,573 | 2,889 | N | N | 8 | 12 |
| S. ATLANTIC | 4,263 | 5,192 | 66,718 | 68,920 | — | — | 161 | 177 |
| Del. | 70 | 76 | 1,339 | 1,198 | N | N | — | — |
| Md. | 513 | 597 | 7,161 | 7,588 | — | — | 9 | 9 |
| D.C. | 276 | 308 | 1,522 | 1,484 | — | — | 2 | 3 |
| Va.¶ | 223 | 282 | 7,944 | 8,960 | — | — | 12 | 23 |
| W. Va. | 22 | 29 | 949 | 1,140 | N | N | 4 | 2 |
| N.C. | 350 | 296 | 13,775 | 11,166 | N | N | 21 | 34 |
| S.C.¶ | 215 | 328 | 8,219 | 7,018 | — | — | 7 | 8 |
| Ga. | 741 | 799 | 8,872 | 13,249 | — | — | 47 | 50 |
| Fla. | 1,853 | 2,477 | 16,937 | 17,117 | N | N | 59 | 48 |
| E.S. CENTRAL | 770 | 774 | 24,698 | 22,814 | — | 3 | 19 | 40 |
| Ky. | 91 | 68 | 4,438 | 2,235 | N | N | 7 | 10 |
| Tenn.¶ | 313 | 324 | 8,895 | 9,220 | N | N | 3 | 12 |
| Ala.¶ | 213 | 203 | 3,346 | 5,599 | — | — | 8 | 10 |
| Miss. | 153 | 179 | 8,019 | 5,760 | — | 3 | 1 | 8 |
| W.S. CENTRAL | 1,513 | 2,023 | 43,292 | 46,910 | — | 2 | 18 | 47 |
| Ark. | 71 | 88 | 3,413 | 3,314 | — | 1 | 1 | 7 |
| La. | 278 | 340 | 7,224 | 10,653 | — | 1 | 3 | — |
| Okla. | 112 | 87 | 4,413 | 4,329 | N | N | 7 | 9 |
| Tex.¶ | 1,052 | 1,508 | 28,242 | 28,614 | N | N | 7 | 31 |
| MOUNTAIN | 537 | 559 | 21,137 | 20,724 | 1,080 | 1,123 | 45 | 41 |
| Mont. | 3 | — | 820 | 903 | N | N | 5 | 7 |
| Idaho¶ | 5 | 3 | 756 | 1,215 | N | N | 2 | 4 |
| Wyo. | — | 6 | 440 | 452 | 1 | — | 2 | 2 |
| Colo. | 107 | 97 | 5,542 | 5,345 | N | N | 18 | 19 |
| N. Mex. | 56 | 90 | 1,478 | 3,497 | 2 | 9 | 2 | 2 |
| Ariz. | 227 | 200 | 8,018 | 5,719 | 1,045 | 1,085 | 4 | 5 |
| Utah | 25 | 32 | 1,717 | 1,354 | 2 | 6 | 7 | 1 |
| Nev.¶ | 114 | 131 | 2,366 | 2,239 | 30 | 23 | 5 | 1 |
| PACIFIC | 1,537 | 2,014 | 61,772 | 62,510 | 539 | 695 | 93 | 104 |
| Wash. | 144 | 165 | 7,762 | 6,983 | N | N | 5 | — |
| Oreg.¶ | 90 | 110 | 3,399 | 3,220 | — | — | 17 | 11 |
| Calif. | 1,250 | 1,685 | 47,351 | 48,356 | 539 | 695 | 71 | 92 |
| Alaska | 9 | 13 | 1,531 | 1,605 | — | — | — | — |
| Hawaii | 44 | 41 | 1,729 | 2,346 | — | — | — | 1 |
| Guam | 1 | — | — | 452 | — | — | — | — |
| P.R. | 335 | 208 | 1,726 | 1,273 | N | N | N | N |
| V.I. | 7 | 5 | 32 | 153 | — | — | — | — |
| Amer. Samoa | U | U | U | U | U | U | U | U |
| C.N.M.I. | 2 | U | — | U | — | U | — | U |

N: Not notifiable. U: Unavailable. —: No reported cases. C.N.M.I.: Commonwealth of Northern Mariana Islands.

* Incidence data for reporting years 2004 and 2005 are provisional and cumulative (year-to-date).

† Chlamydia refers to genital infections caused by *C. trachomatis*.

§ Updated monthly from reports to the Division of HIV/AIDS Prevention, National Center for HIV, STD, and TB Prevention. Last update April 24, 2005.

¶ Contains data reported through National Electronic Disease Surveillance System (NEDSS).

**TABLE II. (*Continued*) Provisional cases of selected notifiable diseases, United States, weeks ending May 28, 2005, and May 29, 2004 (21st Week)***

| Reporting area | *Escherichia coli*, Enterohemorrhagic (EHEC) | | | | | | Giardiasis | | Gonorrhea | |
|---|---|---|---|---|---|---|---|---|---|---|
| | O157:H7 | | Shiga toxin positive, serogroup non-O157 | | Shiga toxin positive, not serogrouped | | | | | |
| | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 |
| UNITED STATES | 411 | 448 | 61 | 79 | 62 | 48 | 5,833 | 6,300 | 114,773 | 127,186 |
| NEW ENGLAND | 29 | 22 | 16 | 19 | 6 | 5 | 463 | 553 | 2,019 | 2,861 |
| Maine | 2 | — | 2 | — | — | — | 44 | 54 | 54 | 107 |
| N.H. | 2 | 4 | 1 | 3 | — | — | 22 | 17 | 62 | 53 |
| Vt. | 2 | — | — | — | — | — | 59 | 42 | 18 | 37 |
| Mass. | 10 | 12 | 5 | 6 | 6 | 5 | 194 | 278 | 1,107 | 1,241 |
| R.I. | 1 | 3 | — | — | — | — | 30 | 47 | 204 | 374 |
| Conn. | 12 | 3 | 8 | 10 | — | — | 114 | 115 | 574 | 1,049 |
| MID. ATLANTIC | 50 | 40 | 3 | 11 | 5 | 10 | 1,093 | 1,405 | 11,887 | 14,654 |
| Upstate N.Y. | 18 | 12 | 3 | 3 | 2 | 3 | 361 | 405 | 2,507 | 2,954 |
| N.Y. City | 2 | 7 | — | — | — | — | 303 | 451 | 3,394 | 4,559 |
| N.J. | 12 | 7 | — | 3 | — | 4 | 146 | 182 | 1,687 | 2,747 |
| Pa. | 18 | 14 | — | 5 | 3 | 3 | 283 | 367 | 4,299 | 4,394 |
| E.N. CENTRAL | 80 | 96 | 8 | 15 | 3 | 5 | 805 | 968 | 21,308 | 26,952 |
| Ohio | 34 | 18 | 1 | 3 | 2 | 5 | 238 | 284 | 6,755 | 8,626 |
| Ind. | 8 | 12 | — | — | — | — | N | N | 3,145 | 2,500 |
| Ill. | 9 | 26 | 1 | — | — | — | 130 | 323 | 5,988 | 7,971 |
| Mich. | 14 | 17 | — | 2 | 1 | — | 250 | 213 | 3,510 | 6,036 |
| Wis. | 15 | 23 | 6 | 10 | — | — | 187 | 148 | 1,910 | 1,819 |
| W.N. CENTRAL | 60 | 70 | 13 | 14 | 9 | 9 | 745 | 676 | 6,611 | 6,673 |
| Minn. | 8 | 24 | 4 | 6 | 2 | 2 | 382 | 206 | 895 | 1,160 |
| Iowa | 12 | 12 | — | — | — | — | 77 | 96 | 609 | 503 |
| Mo. | 23 | 10 | 6 | 6 | 2 | 2 | 154 | 207 | 3,724 | 3,420 |
| N. Dak. | 1 | 2 | — | — | — | 3 | 1 | 11 | 19 | 58 |
| S. Dak. | 2 | 3 | — | — | — | — | 33 | 22 | 150 | 105 |
| Nebr. | 5 | 9 | 3 | 2 | 2 | — | 38 | 57 | 349 | 436 |
| Kans. | 9 | 10 | — | — | 3 | 2 | 60 | 77 | 865 | 991 |
| S. ATLANTIC | 63 | 43 | 11 | 11 | 31 | 8 | 998 | 986 | 28,296 | 30,350 |
| Del. | — | — | N | N | N | N | 8 | 20 | 318 | 388 |
| Md. | 6 | 5 | 2 | 2 | 1 | 2 | 59 | 36 | 2,649 | 3,180 |
| D.C. | — | 1 | — | — | — | — | 18 | 30 | 817 | 998 |
| Va. | 3 | 1 | 4 | 6 | 6 | — | 204 | 141 | 2,865 | 3,595 |
| W. Va. | — | 1 | — | — | — | — | 11 | 12 | 277 | 332 |
| N.C. | — | — | — | — | 16 | 4 | N | N | 6,613 | 5,885 |
| S.C. | 1 | 4 | — | — | — | — | 30 | 37 | 3,514 | 3,387 |
| Ga. | 8 | 13 | 3 | 1 | — | — | 360 | 305 | 3,850 | 5,591 |
| Fla. | 45 | 18 | 2 | 2 | 8 | 2 | 308 | 405 | 7,393 | 6,994 |
| E.S. CENTRAL | 22 | 26 | — | 2 | 5 | 6 | 144 | 139 | 9,043 | 9,893 |
| Ky. | 4 | 8 | — | 1 | 4 | 4 | N | N | 1,394 | 946 |
| Tenn. | 11 | 3 | — | — | 1 | 2 | 74 | 66 | 3,153 | 3,251 |
| Ala. | 7 | 7 | — | — | — | — | 70 | 73 | 2,072 | 3,211 |
| Miss. | — | 8 | — | 1 | — | — | — | — | 2,424 | 2,485 |
| W.S. CENTRAL | 9 | 43 | 1 | 2 | 2 | 5 | 89 | 107 | 16,919 | 17,383 |
| Ark. | 1 | 8 | — | — | — | — | 30 | 47 | 1,723 | 1,604 |
| La. | 2 | 1 | 1 | — | 2 | — | 13 | 17 | 3,980 | 4,777 |
| Okla. | 3 | 4 | — | — | — | — | 46 | 43 | 1,839 | 1,847 |
| Tex. | 3 | 30 | — | 2 | — | 5 | N | N | 9,377 | 9,155 |
| MOUNTAIN | 44 | 45 | 9 | 4 | 1 | — | 431 | 449 | 4,278 | 4,552 |
| Mont. | 3 | 3 | — | — | — | — | 13 | 15 | 44 | 31 |
| Idaho | 3 | 12 | 5 | 1 | — | — | 31 | 64 | 32 | 34 |
| Wyo. | — | — | 1 | — | — | — | 10 | 7 | 26 | 23 |
| Colo. | 13 | 9 | 1 | 1 | — | — | 152 | 150 | 1,092 | 1,289 |
| N. Mex. | — | 5 | 2 | 1 | — | — | 14 | 25 | 260 | 407 |
| Ariz. | 10 | 6 | N | N | N | N | 59 | 71 | 1,690 | 1,618 |
| Utah | 7 | 6 | — | — | — | — | 124 | 93 | 268 | 193 |
| Nev. | 8 | 4 | — | 1 | 1 | — | 28 | 24 | 866 | 957 |
| PACIFIC | 54 | 63 | — | 1 | — | — | 1,065 | 1,017 | 14,412 | 13,868 |
| Wash. | 15 | 17 | — | — | — | — | 87 | 94 | 1,413 | 1,061 |
| Oreg. | 6 | 8 | — | 1 | — | — | 92 | 153 | 618 | 407 |
| Calif. | 27 | 34 | — | — | — | — | 833 | 710 | 11,868 | 11,566 |
| Alaska | 3 | 1 | — | — | — | — | 30 | 26 | 196 | 272 |
| Hawaii | 3 | 3 | — | — | — | — | 23 | 34 | 317 | 562 |
| Guam | N | N | — | — | — | — | — | — | — | 71 |
| P.R. | — | — | — | — | — | — | 10 | 25 | 161 | 107 |
| V.I. | — | — | — | — | — | — | — | — | 2 | 53 |
| Amer. Samoa | U | U | U | U | U | U | U | U | U | U |
| C.N.M.I. | — | U | — | U | — | U | — | U | — | U |

N: Not notifiable. U: Unavailable. —: No reported cases. C.N.M.I.: Commonwealth of Northern Mariana Islands.
* Incidence data for reporting years 2004 and 2005 are provisional and cumulative (year-to-date).

**TABLE II. (*Continued*) Provisional cases of selected notifiable diseases, United States, weeks ending May 28, 2005, and May 29, 2004 (21st Week)***

| Reporting area | *Haemophilus influenzae*, invasive | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | All ages | | Age <5 years | | | | | |
| | All serotypes | | Serotype b | | Non-serotype b | | Unknown serotype | |
| | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 |
| UNITED STATES | 947 | 931 | 2 | 6 | 53 | 48 | 88 | 94 |
| NEW ENGLAND | 68 | 93 | — | 1 | 6 | 6 | 3 | 1 |
| Maine | 3 | 7 | — | — | — | — | 1 | — |
| N.H. | 3 | 12 | — | — | — | 2 | — | — |
| Vt. | 6 | 5 | — | — | — | — | 2 | 1 |
| Mass. | 27 | 44 | — | 1 | 1 | 2 | — | — |
| R.I. | 6 | 2 | — | — | 2 | — | — | — |
| Conn. | 23 | 23 | — | — | 3 | 2 | — | — |
| MID. ATLANTIC | 188 | 190 | — | 1 | — | 3 | 21 | 24 |
| Upstate N.Y. | 51 | 64 | — | 1 | — | 3 | 5 | 3 |
| N.Y. City | 31 | 42 | — | — | — | — | 6 | 8 |
| N.J. | 38 | 34 | — | — | — | — | 5 | 2 |
| Pa. | 68 | 50 | — | — | — | — | 5 | 11 |
| E.N. CENTRAL | 128 | 169 | — | — | 1 | 8 | 7 | 24 |
| Ohio | 67 | 58 | — | — | — | 2 | 6 | 10 |
| Ind. | 35 | 26 | — | — | 1 | 4 | 1 | 1 |
| Ill. | 9 | 50 | — | — | — | — | — | 10 |
| Mich. | 10 | 10 | — | — | — | 2 | — | 3 |
| Wis. | 7 | 25 | — | — | — | — | — | — |
| W.N. CENTRAL | 49 | 43 | — | 1 | 2 | 2 | 7 | 5 |
| Minn. | 18 | 14 | — | — | 2 | 2 | — | — |
| Iowa | — | 1 | — | 1 | — | — | — | — |
| Mo. | 24 | 18 | — | — | — | — | 5 | 4 |
| N. Dak. | 1 | 3 | — | — | — | — | 1 | — |
| S. Dak. | — | — | — | — | — | — | — | — |
| Nebr. | 3 | 2 | — | — | — | — | 1 | — |
| Kans. | 3 | 5 | — | — | — | — | — | 1 |
| S. ATLANTIC | 244 | 216 | — | — | 14 | 11 | 13 | 16 |
| Del. | — | — | — | — | — | — | — | — |
| Md. | 35 | 39 | — | — | 4 | 2 | — | — |
| D.C. | — | 1 | — | — | — | — | — | 1 |
| Va. | 19 | 18 | — | — | — | — | — | 1 |
| W. Va. | 14 | 10 | — | — | 1 | 3 | 2 | — |
| N.C. | 40 | 25 | — | — | 5 | 3 | — | — |
| S.C. | 10 | 5 | — | — | — | — | 1 | — |
| Ga. | 61 | 65 | — | — | — | — | 6 | 14 |
| Fla. | 65 | 53 | — | — | 4 | 3 | 4 | — |
| E.S. CENTRAL | 46 | 35 | — | — | 1 | — | 10 | 6 |
| Ky. | 4 | — | — | — | 1 | — | 1 | — |
| Tenn. | 32 | 25 | — | — | — | — | 6 | 4 |
| Ala. | 10 | 10 | — | — | — | — | 3 | 2 |
| Miss. | — | — | — | — | — | — | — | — |
| W.S. CENTRAL | 59 | 37 | 1 | 1 | 4 | 4 | 6 | 1 |
| Ark. | — | 1 | — | — | — | — | — | — |
| La. | 26 | 9 | 1 | — | 2 | — | 6 | 1 |
| Okla. | 33 | 26 | — | — | 2 | 4 | — | — |
| Tex. | — | 1 | — | 1 | — | — | — | — |
| MOUNTAIN | 122 | 105 | — | 2 | 14 | 10 | 18 | 12 |
| Mont. | — | — | — | — | — | — | — | — |
| Idaho | 3 | 4 | — | — | — | — | 1 | 2 |
| Wyo. | 1 | — | — | — | — | — | — | — |
| Colo. | 27 | 25 | — | — | — | — | 4 | 3 |
| N. Mex. | 13 | 23 | — | — | 4 | 3 | 1 | 4 |
| Ariz. | 55 | 43 | — | — | 8 | 6 | 4 | 1 |
| Utah | 10 | 8 | — | 2 | — | 1 | 6 | 1 |
| Nev. | 13 | 2 | — | — | 2 | — | 2 | 1 |
| PACIFIC | 43 | 43 | 1 | — | 11 | 4 | 3 | 5 |
| Wash. | — | 1 | — | — | — | — | — | 1 |
| Oreg. | 18 | 22 | — | — | — | — | 3 | 2 |
| Calif. | 19 | 13 | 1 | — | 11 | 4 | — | 1 |
| Alaska | 1 | 3 | — | — | — | — | — | 1 |
| Hawaii | 5 | 4 | — | — | — | — | — | — |
| Guam | — | — | — | — | — | — | — | — |
| P.R. | — | — | — | — | — | — | — | — |
| V.I. | — | — | — | — | — | — | — | — |
| Amer. Samoa | U | U | U | U | U | U | U | U |
| C.N.M.I. | — | U | — | U | — | U | — | U |

N: Not notifiable. U: Unavailable. —: No reported cases. C.N.M.I.: Commonwealth of Northern Mariana Islands.
* Incidence data for reporting years 2004 and 2005 are provisional and cumulative (year-to-date).

**TABLE II. (*Continued*) Provisional cases of selected notifiable diseases, United States, weeks ending May 28, 2005, and May 29, 2004 (21st Week)***

| Reporting area | Hepatitis (viral, acute), by type | | | | | |
|---|---|---|---|---|---|---|
| | A | | B | | C | |
| | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 |
| UNITED STATES | 1,466 | 2,449 | 2,238 | 2,313 | 253 | 289 |
| NEW ENGLAND | 200 | 334 | 118 | 149 | 6 | 4 |
| Maine | — | 7 | 4 | 1 | — | — |
| N.H. | 24 | 8 | 5 | 20 | — | — |
| Vt. | 1 | 5 | 1 | 2 | 6 | 1 |
| Mass. | 147 | 279 | 93 | 71 | — | 3 |
| R.I. | 5 | 7 | — | 2 | — | — |
| Conn. | 23 | 28 | 15 | 53 | U | — |
| MID. ATLANTIC | 242 | 290 | 488 | 304 | 42 | 46 |
| Upstate N.Y. | 37 | 34 | 43 | 33 | 10 | 2 |
| N.Y. City | 118 | 110 | 39 | 66 | — | — |
| N.J. | 41 | 64 | 322 | 79 | — | — |
| Pa. | 46 | 82 | 84 | 126 | 32 | 44 |
| E.N. CENTRAL | 142 | 188 | 153 | 221 | 47 | 30 |
| Ohio | 25 | 23 | 60 | 57 | 2 | 2 |
| Ind. | 20 | 19 | 10 | 13 | 9 | 2 |
| Ill. | 27 | 59 | 14 | 21 | — | 7 |
| Mich. | 56 | 67 | 69 | 109 | 36 | 19 |
| Wis. | 14 | 20 | — | 21 | — | — |
| W.N. CENTRAL | 49 | 57 | 142 | 137 | 15 | 1 |
| Minn. | 3 | 10 | 8 | 12 | — | 1 |
| Iowa | 10 | 18 | 39 | 7 | — | — |
| Mo. | 27 | 9 | 70 | 97 | 14 | — |
| N. Dak. | — | 1 | — | 1 | 1 | — |
| S. Dak. | — | 2 | — | — | — | — |
| Nebr. | 2 | 10 | 13 | 11 | — | — |
| Kans. | 7 | 7 | 12 | 9 | — | — |
| S. ATLANTIC | 212 | 419 | 643 | 742 | 52 | 73 |
| Del. | — | 4 | 26 | 17 | — | 2 |
| Md. | 21 | 58 | 79 | 60 | 13 | 1 |
| D.C. | 2 | 4 | — | 12 | — | 1 |
| Va. | 29 | 33 | 75 | 80 | 6 | 7 |
| W. Va. | 2 | 1 | 14 | 2 | 5 | 10 |
| N.C. | 29 | 29 | 67 | 74 | 7 | 6 |
| S.C. | 8 | 22 | 41 | 51 | 1 | 6 |
| Ga. | 40 | 163 | 116 | 228 | 3 | 7 |
| Fla. | 81 | 105 | 225 | 218 | 17 | 33 |
| E.S. CENTRAL | 88 | 67 | 133 | 195 | 28 | 29 |
| Ky. | 4 | 9 | 29 | 22 | 1 | 13 |
| Tenn. | 61 | 46 | 58 | 89 | 7 | 7 |
| Ala. | 11 | 6 | 29 | 31 | 8 | 1 |
| Miss. | 12 | 6 | 17 | 53 | 12 | 8 |
| W.S. CENTRAL | 87 | 450 | 101 | 105 | 25 | 65 |
| Ark. | 2 | 46 | 17 | 51 | — | — |
| La. | 28 | 13 | 20 | 24 | 6 | 3 |
| Okla. | 3 | 16 | 7 | 24 | — | 2 |
| Tex. | 54 | 375 | 57 | 6 | 19 | 60 |
| MOUNTAIN | 144 | 185 | 212 | 166 | 16 | 17 |
| Mont. | 6 | 3 | 2 | 1 | — | 2 |
| Idaho | 12 | 10 | 5 | 6 | — | 1 |
| Wyo. | — | — | — | 3 | — | — |
| Colo. | 15 | 18 | 18 | 21 | 7 | 4 |
| N. Mex. | 7 | 6 | 5 | 10 | — | 5 |
| Ariz. | 86 | 127 | 146 | 82 | — | 2 |
| Utah | 12 | 19 | 24 | 17 | 6 | 1 |
| Nev. | 6 | 2 | 12 | 26 | 3 | 2 |
| PACIFIC | 302 | 459 | 248 | 294 | 22 | 24 |
| Wash. | 19 | 26 | 24 | 23 | 3 | 6 |
| Oreg. | 17 | 35 | 40 | 41 | 9 | 7 |
| Calif. | 254 | 385 | 178 | 219 | 10 | 11 |
| Alaska | 3 | 3 | 5 | 8 | — | — |
| Hawaii | 9 | 10 | 1 | 3 | — | — |
| Guam | — | 1 | — | 4 | — | — |
| P.R. | 2 | 11 | 3 | 21 | — | — |
| V.I. | — | — | — | — | — | — |
| Amer. Samoa | U | U | U | U | U | U |
| C.N.M.I. | — | U | — | U | — | U |

N: Not notifiable. U: Unavailable. —: No reported cases. C.N.M.I.: Commonwealth of Northern Mariana Islands.
* Incidence data for reporting years 2004 and 2005 are provisional and cumulative (year-to-date).

**TABLE II. (*Continued*) Provisional cases of selected notifiable diseases, United States, weeks ending May 28, 2005, and May 29, 2004 (21st Week)***

| Reporting area | Legionellosis | | Listeriosis | | Lyme disease | | Malaria | |
|---|---|---|---|---|---|---|---|---|
| | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 |
| UNITED STATES | 419 | 495 | 180 | 211 | 2,101 | 3,310 | 374 | 486 |
| NEW ENGLAND | 23 | 9 | 6 | 11 | 121 | 436 | 15 | 38 |
| Maine | 1 | — | — | 2 | 2 | 24 | — | 3 |
| N.H. | 4 | — | 1 | 1 | 20 | 18 | 3 | — |
| Vt. | — | — | — | — | 2 | 11 | — | 1 |
| Mass. | 12 | 4 | 2 | 3 | 69 | 261 | 10 | 23 |
| R.I. | 1 | 1 | 1 | 1 | 3 | 32 | 2 | 2 |
| Conn. | 5 | 4 | 2 | 4 | 25 | 90 | — | 9 |
| MID. ATLANTIC | 121 | 92 | 35 | 47 | 1,469 | 2,282 | 103 | 120 |
| Upstate N.Y. | 30 | 19 | 9 | 12 | 254 | 813 | 19 | 14 |
| N.Y. City | 14 | 11 | 7 | 7 | — | 72 | 44 | 60 |
| N.J. | 27 | 14 | 7 | 16 | 655 | 548 | 27 | 24 |
| Pa. | 50 | 48 | 12 | 12 | 560 | 849 | 13 | 22 |
| E.N. CENTRAL | 89 | 102 | 19 | 28 | 34 | 155 | 21 | 33 |
| Ohio | 43 | 42 | 7 | 9 | 22 | 17 | 5 | 9 |
| Ind. | 6 | 10 | 1 | 6 | 2 | 1 | — | 4 |
| Ill. | 9 | 17 | — | 5 | — | 23 | 5 | 9 |
| Mich. | 23 | 28 | 6 | 6 | 2 | — | 8 | 7 |
| Wis. | 8 | 5 | 5 | 2 | 8 | 114 | 3 | 4 |
| W.N. CENTRAL | 13 | 12 | 11 | 3 | 76 | 41 | 19 | 24 |
| Minn. | 1 | — | 2 | 1 | 60 | 12 | 8 | 9 |
| Iowa | 2 | 3 | 4 | 1 | 9 | 10 | 2 | 1 |
| Mo. | 8 | 5 | 2 | 1 | 6 | 14 | 8 | 5 |
| N. Dak. | 1 | 1 | 2 | — | — | — | — | 2 |
| S. Dak. | — | 1 | — | — | — | — | — | 1 |
| Nebr. | — | 1 | — | — | — | 4 | — | 1 |
| Kans. | 1 | 1 | 1 | — | 1 | 1 | 1 | 5 |
| S. ATLANTIC | 85 | 108 | 43 | 28 | 341 | 325 | 86 | 123 |
| Del. | 1 | 2 | N | N | 77 | 47 | — | 3 |
| Md. | 19 | 15 | 5 | 5 | 184 | 198 | 27 | 26 |
| D.C. | 1 | 3 | — | — | 3 | 2 | 2 | 6 |
| Va. | 6 | 8 | 2 | 3 | 28 | 13 | 9 | 10 |
| W. Va. | 4 | 2 | — | 1 | 3 | 2 | 1 | — |
| N.C. | 10 | 9 | 9 | 5 | 18 | 37 | 13 | 8 |
| S.C. | 2 | 2 | 1 | — | 7 | 3 | 3 | 7 |
| Ga. | 6 | 19 | 9 | 7 | — | 7 | 14 | 23 |
| Fla. | 36 | 48 | 17 | 7 | 21 | 16 | 17 | 40 |
| E.S. CENTRAL | 11 | 21 | 9 | 11 | 11 | 13 | 11 | 14 |
| Ky. | 2 | 5 | 1 | 3 | — | 5 | 2 | 1 |
| Tenn. | 3 | 9 | 4 | 6 | 11 | 6 | 6 | 3 |
| Ala. | 6 | 6 | 3 | 1 | — | 2 | 3 | 7 |
| Miss. | — | 1 | 1 | 1 | — | — | — | 3 |
| W.S. CENTRAL | 11 | 100 | 5 | 36 | 15 | 26 | 22 | 62 |
| Ark. | 1 | — | — | 1 | 2 | — | 1 | 3 |
| La. | 4 | 5 | 3 | 2 | 3 | 1 | — | 3 |
| Okla. | 1 | 2 | — | — | — | — | 2 | 1 |
| Tex. | 5 | 93 | 2 | 33 | 10 | 25 | 19 | 55 |
| MOUNTAIN | 40 | 27 | 1 | 4 | 2 | 5 | 18 | 15 |
| Mont. | 2 | 1 | — | — | — | — | — | — |
| Idaho | 1 | 1 | — | 1 | — | 2 | — | 1 |
| Wyo. | 2 | 4 | — | — | — | 2 | 1 | — |
| Colo. | 10 | 4 | 1 | 1 | — | — | 11 | 6 |
| N. Mex. | 1 | — | — | — | — | — | — | 1 |
| Ariz. | 12 | 5 | — | — | — | 1 | 2 | 2 |
| Utah | 5 | 9 | — | — | 2 | — | 4 | 3 |
| Nev. | 7 | 3 | — | 2 | — | — | — | 2 |
| PACIFIC | 26 | 24 | 51 | 43 | 32 | 27 | 79 | 57 |
| Wash. | — | 4 | 2 | 6 | — | 2 | 7 | 1 |
| Oreg. | N | N | 4 | 4 | 2 | 14 | 1 | 8 |
| Calif. | 26 | 20 | 45 | 33 | 29 | 11 | 65 | 46 |
| Alaska | — | — | — | — | 1 | — | 2 | — |
| Hawaii | — | — | — | — | N | N | 4 | 2 |
| Guam | — | — | — | — | — | — | — | — |
| P.R. | — | 1 | — | — | N | N | — | — |
| V.I. | — | — | — | — | — | — | — | — |
| Amer. Samoa | U | U | U | U | U | U | U | U |
| C.N.M.I. | — | U | — | U | — | U | — | U |

N: Not notifiable. U: Unavailable. —: No reported cases. C.N.M.I.: Commonwealth of Northern Mariana Islands.
* Incidence data for reporting years 2004 and 2005 are provisional and cumulative (year-to-date).

**TABLE II. (*Continued*) Provisional cases of selected notifiable diseases, United States, weeks ending May 28, 2005, and May 29, 2004 (21st Week)***

| Reporting area | Meningococcal disease | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | All serogroups | | Serogroup A, C, Y, and W-135 | | Serogroup B | | Other serogroup | | Serogroup unknown | |
| | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 |
| UNITED STATES | 554 | 636 | 44 | 42 | 27 | 26 | — | — | 483 | 568 |
| NEW ENGLAND | 38 | 33 | 1 | 4 | — | 4 | — | — | 37 | 25 |
| Maine | 1 | 8 | — | — | — | 1 | — | — | 1 | 7 |
| N.H. | 5 | 3 | — | — | — | — | — | — | 5 | 3 |
| Vt. | 3 | 1 | — | — | — | — | — | — | 3 | 1 |
| Mass. | 18 | 20 | — | 4 | — | 3 | — | — | 18 | 13 |
| R.I. | 2 | — | — | — | — | — | — | — | 2 | — |
| Conn. | 9 | 1 | 1 | — | — | — | — | — | 8 | 1 |
| MID. ATLANTIC | 75 | 88 | 22 | 25 | 4 | 5 | — | — | 49 | 58 |
| Upstate N.Y. | 19 | 25 | 2 | 4 | 3 | 3 | — | — | 14 | 18 |
| N.Y. City | 10 | 15 | — | — | — | — | — | — | 10 | 15 |
| N.J. | 20 | 17 | — | — | — | — | — | — | 20 | 17 |
| Pa. | 26 | 31 | 20 | 21 | 1 | 2 | — | — | 5 | 8 |
| E.N. CENTRAL | 53 | 60 | 13 | 8 | 4 | 4 | — | — | 36 | 48 |
| Ohio | 25 | 37 | — | 3 | 4 | 4 | — | — | 21 | 30 |
| Ind. | 8 | 8 | — | — | — | — | — | — | 8 | 8 |
| Ill. | 2 | 1 | — | — | — | — | — | — | 2 | 1 |
| Mich. | 13 | 5 | 13 | 5 | — | — | — | — | — | — |
| Wis. | 5 | 9 | — | — | — | — | — | — | 5 | 9 |
| W.N. CENTRAL | 32 | 37 | 2 | — | 1 | 3 | — | — | 29 | 34 |
| Minn. | 6 | 9 | 1 | — | — | — | — | — | 5 | 9 |
| Iowa | 9 | 8 | — | — | 1 | 2 | — | — | 8 | 6 |
| Mo. | 10 | 11 | 1 | — | — | 1 | — | — | 9 | 10 |
| N. Dak. | — | 1 | — | — | — | — | — | — | — | 1 |
| S. Dak. | 1 | 1 | — | — | — | — | — | — | 1 | 1 |
| Nebr. | 2 | 3 | — | — | — | — | — | — | 2 | 3 |
| Kans. | 4 | 4 | — | — | — | — | — | — | 4 | 4 |
| S. ATLANTIC | 99 | 124 | 2 | 2 | 4 | 2 | — | — | 93 | 120 |
| Del. | — | 1 | — | — | — | — | — | — | — | 1 |
| Md. | 9 | 7 | 1 | — | 2 | — | — | — | 6 | 7 |
| D.C. | — | 5 | — | 2 | — | — | — | — | — | 3 |
| Va. | 12 | 8 | — | — | — | — | — | — | 12 | 8 |
| W. Va. | 4 | 4 | — | — | — | — | — | — | 4 | 4 |
| N.C. | 11 | 18 | 1 | — | 2 | 2 | — | — | 8 | 16 |
| S.C. | 11 | 12 | — | — | — | — | — | — | 11 | 12 |
| Ga. | 10 | 8 | — | — | — | — | — | — | 10 | 8 |
| Fla. | 42 | 61 | — | — | — | — | — | — | 42 | 61 |
| E.S. CENTRAL | 27 | 29 | — | — | 2 | — | — | — | 25 | 29 |
| Ky. | 8 | 3 | — | — | 2 | — | — | — | 6 | 3 |
| Tenn. | 13 | 10 | — | — | — | — | — | — | 13 | 10 |
| Ala. | 2 | 6 | — | — | — | — | — | — | 2 | 6 |
| Miss. | 4 | 10 | — | — | — | — | — | — | 4 | 10 |
| W.S. CENTRAL | 45 | 59 | 1 | 1 | 3 | 1 | — | — | 41 | 57 |
| Ark. | 8 | 10 | — | — | — | — | — | — | 8 | 10 |
| La. | 20 | 21 | — | 1 | 2 | — | — | — | 18 | 20 |
| Okla. | 9 | 3 | 1 | — | 1 | 1 | — | — | 7 | 2 |
| Tex. | 8 | 25 | — | — | — | — | — | — | 8 | 25 |
| MOUNTAIN | 45 | 30 | 2 | — | 4 | 3 | — | — | 39 | 27 |
| Mont. | — | 1 | — | — | — | — | — | — | — | 1 |
| Idaho | 1 | 4 | — | — | — | — | — | — | 1 | 4 |
| Wyo. | — | 3 | — | — | — | — | — | — | — | 3 |
| Colo. | 12 | 9 | 2 | — | — | — | — | — | 10 | 9 |
| N. Mex. | 1 | 4 | — | — | — | 2 | — | — | 1 | 2 |
| Ariz. | 21 | 5 | — | — | 2 | — | — | — | 19 | 5 |
| Utah | 7 | 2 | — | — | 2 | — | — | — | 5 | 2 |
| Nev. | 3 | 2 | — | — | — | 1 | — | — | 3 | 1 |
| PACIFIC | 140 | 176 | 1 | 2 | 5 | 4 | — | — | 134 | 170 |
| Wash. | 28 | 16 | 1 | 2 | 4 | 4 | — | — | 23 | 10 |
| Oreg. | 23 | 35 | — | — | — | — | — | — | 23 | 35 |
| Calif. | 82 | 118 | — | — | — | — | — | — | 82 | 118 |
| Alaska | 1 | 2 | — | — | — | — | — | — | 1 | 2 |
| Hawaii | 6 | 5 | — | — | 1 | — | — | — | 5 | 5 |
| Guam | — | — | — | — | — | — | — | — | — | — |
| P.R. | 3 | 5 | — | — | — | — | — | — | 3 | 5 |
| V.I. | — | — | — | — | — | — | — | — | — | — |
| Amer. Samoa | — | — | — | — | — | — | — | — | — | — |
| C.N.M.I. | — | — | — | — | — | — | — | — | — | — |

N: Not notifiable. U: Unavailable. —: No reported cases. C.N.M.I.: Commonwealth of Northern Mariana Islands.
* Incidence data for reporting years 2004 and 2005 are provisional and cumulative (year-to-date).

**TABLE II. (*Continued*) Provisional cases of selected notifiable diseases, United States, weeks ending May 28, 2005, and May 29, 2004 (21st Week)***

| Reporting area | Pertussis | | Rabies, animal | | Rocky Mountain spotted fever | | Salmonellosis | | Shigellosis | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 |
| UNITED STATES | 6,332 | 4,089 | 1,957 | 2,764 | 233 | 246 | 9,575 | 11,260 | 3,704 | 5,281 |
| NEW ENGLAND | 322 | 600 | 291 | 193 | 1 | 5 | 582 | 513 | 73 | 91 |
| Maine | 12 | 3 | 19 | 22 | N | N | 26 | 31 | 2 | 1 |
| N.H. | 17 | 21 | 4 | 6 | — | — | 41 | 34 | 4 | 4 |
| Vt. | 46 | 39 | 22 | 6 | — | — | 34 | 18 | 4 | 2 |
| Mass. | 225 | 509 | 178 | 85 | — | 5 | 322 | 283 | 42 | 59 |
| R.I. | 8 | 9 | 6 | 11 | 1 | — | 19 | 37 | 2 | 4 |
| Conn. | 14 | 19 | 62 | 63 | — | — | 140 | 110 | 19 | 21 |
| MID. ATLANTIC | 604 | 909 | 213 | 288 | 15 | 25 | 1,224 | 1,426 | 406 | 489 |
| Upstate N.Y. | 206 | 647 | 161 | 140 | — | 1 | 325 | 328 | 99 | 210 |
| N.Y. City | 28 | 66 | 9 | 5 | 1 | 8 | 305 | 418 | 169 | 146 |
| N.J. | 109 | 65 | N | N | 5 | 6 | 202 | 254 | 109 | 85 |
| Pa. | 261 | 131 | 43 | 143 | 9 | 10 | 392 | 426 | 29 | 48 |
| E.N. CENTRAL | 1,493 | 917 | 38 | 19 | 6 | 10 | 1,012 | 1,561 | 235 | 340 |
| Ohio | 632 | 166 | 21 | 7 | 5 | 4 | 307 | 361 | 24 | 70 |
| Ind. | 138 | 34 | 3 | 3 | — | 1 | 123 | 158 | 33 | 58 |
| Ill. | 83 | 180 | 8 | 4 | — | 4 | 108 | 506 | 24 | 132 |
| Mich. | 100 | 42 | 6 | 3 | 1 | 1 | 247 | 266 | 96 | 34 |
| Wis. | 540 | 495 | — | 2 | — | — | 227 | 270 | 58 | 46 |
| W.N. CENTRAL | 854 | 242 | 133 | 228 | 29 | 16 | 691 | 713 | 293 | 140 |
| Minn. | 159 | 41 | 30 | 18 | — | — | 183 | 181 | 26 | 18 |
| Iowa | 289 | 39 | 29 | 23 | — | — | 109 | 136 | 41 | 29 |
| Mo. | 183 | 133 | 20 | 7 | 27 | 14 | 211 | 191 | 182 | 53 |
| N. Dak. | 48 | 6 | 6 | 23 | — | — | 11 | 13 | 2 | 1 |
| S. Dak. | 1 | 8 | 12 | 47 | — | — | 45 | 25 | 8 | 6 |
| Nebr. | 72 | 4 | — | 60 | 1 | 2 | 48 | 53 | 20 | 7 |
| Kans. | 102 | 11 | 36 | 50 | 1 | — | 84 | 114 | 14 | 26 |
| S. ATLANTIC | 459 | 221 | 646 | 1,008 | 136 | 132 | 2,680 | 2,284 | 667 | 1,186 |
| Del. | 12 | — | — | 9 | 1 | 2 | 13 | 19 | 4 | 3 |
| Md. | 78 | 50 | 109 | 119 | 14 | 5 | 216 | 195 | 28 | 46 |
| D.C. | 3 | 6 | — | — | — | — | 14 | 15 | 6 | 21 |
| Va. | 74 | 59 | 232 | 187 | 4 | 1 | 268 | 251 | 35 | 36 |
| W. Va. | 22 | 3 | 13 | 29 | 1 | — | 35 | 46 | — | — |
| N.C. | 27 | 33 | 198 | 268 | 87 | 87 | 423 | 279 | 63 | 133 |
| S.C. | 161 | 30 | 5 | 60 | 6 | 13 | 161 | 140 | 35 | 211 |
| Ga. | 15 | 12 | 86 | 131 | 14 | 21 | 445 | 398 | 190 | 270 |
| Fla. | 67 | 28 | 3 | 205 | 9 | 3 | 1,105 | 941 | 306 | 466 |
| E.S. CENTRAL | 174 | 48 | 54 | 55 | 14 | 32 | 523 | 629 | 515 | 236 |
| Ky. | 49 | 8 | 6 | 11 | — | — | 95 | 104 | 43 | 31 |
| Tenn. | 78 | 26 | 18 | 17 | 11 | 19 | 187 | 184 | 302 | 93 |
| Ala. | 34 | 7 | 30 | 22 | 3 | 6 | 171 | 178 | 135 | 87 |
| Miss. | 13 | 7 | — | 5 | — | 7 | 70 | 163 | 35 | 25 |
| W.S. CENTRAL | 150 | 154 | 458 | 854 | 8 | 20 | 616 | 1,598 | 680 | 1,958 |
| Ark. | 74 | 14 | 13 | 24 | 2 | 4 | 122 | 121 | 20 | 18 |
| La. | 14 | 7 | — | — | 1 | 3 | 189 | 192 | 44 | 133 |
| Okla. | — | 13 | 48 | 54 | 5 | 13 | 101 | 100 | 293 | 196 |
| Tex. | 62 | 120 | 397 | 776 | — | — | 204 | 1,185 | 323 | 1,611 |
| MOUNTAIN | 1,524 | 422 | 74 | 46 | 20 | 3 | 654 | 737 | 216 | 275 |
| Mont. | 323 | 12 | — | 5 | 1 | — | 33 | 51 | 2 | 3 |
| Idaho | 46 | 17 | — | — | — | 1 | 30 | 55 | — | 5 |
| Wyo. | 13 | 3 | 11 | — | 1 | — | 16 | 20 | — | 1 |
| Colo. | 642 | 225 | 5 | 5 | 2 | 1 | 166 | 174 | 38 | 49 |
| N. Mex. | 52 | 62 | — | — | — | — | 48 | 81 | 28 | 52 |
| Ariz. | 261 | 72 | 58 | 36 | 13 | 1 | 201 | 231 | 107 | 132 |
| Utah | 169 | 29 | — | — | 3 | — | 105 | 80 | 16 | 15 |
| Nev. | 18 | 2 | — | — | — | — | 55 | 45 | 25 | 18 |
| PACIFIC | 752 | 576 | 50 | 73 | 4 | 3 | 1,593 | 1,799 | 619 | 566 |
| Wash. | 164 | 161 | — | — | — | — | 137 | 120 | 24 | 31 |
| Oreg. | 267 | 195 | — | — | — | 2 | 110 | 153 | 24 | 30 |
| Calif. | 260 | 202 | 49 | 62 | 4 | 1 | 1,227 | 1,370 | 555 | 485 |
| Alaska | 16 | 10 | 1 | 11 | — | — | 17 | 28 | 5 | 4 |
| Hawaii | 45 | 8 | — | — | — | — | 102 | 128 | 11 | 16 |
| Guam | — | — | — | — | — | — | — | 16 | — | 17 |
| P.R. | — | 1 | 28 | 18 | N | N | 29 | 78 | — | 1 |
| V.I. | — | — | — | — | — | — | — | — | — | — |
| Amer. Samoa | U | U | U | U | U | U | U | U | U | U |
| C.N.M.I. | — | U | — | U | — | U | — | U | — | U |

N: Not notifiable. U: Unavailable. —: No reported cases. C.N.M.I.: Commonwealth of Northern Mariana Islands.
* Incidence data for reporting years 2004 and 2005 are provisional and cumulative (year-to-date).

**TABLE II. (*Continued*) Provisional cases of selected notifiable diseases, United States, weeks ending May 28, 2005, and May 29, 2004 (21st Week)***

| Reporting area | Streptococcal disease, invasive, group A | | *Streptococcus pneumoniae*, invasive disease | | | | Syphilis | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Drug resistant, all ages | | Age <5 years | | Primary & secondary | | Congenital | |
| | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 |
| UNITED STATES | 2,029 | 2,427 | 1,182 | 1,219 | 370 | 404 | 2,783 | 3,030 | 101 | 161 |
| NEW ENGLAND | 72 | 169 | 12 | 59 | 37 | 58 | 76 | 73 | — | — |
| Maine | 2 | 3 | N | N | — | 1 | 1 | — | — | — |
| N.H. | 6 | 11 | — | — | 2 | N | 5 | 2 | — | — |
| Vt. | 7 | 5 | 6 | 5 | 3 | 1 | — | — | — | — |
| Mass. | 51 | 81 | — | 11 | 32 | 36 | 59 | 44 | — | — |
| R.I. | 6 | 16 | 6 | 7 | — | 3 | 2 | 9 | — | — |
| Conn. | — | 53 | U | 36 | U | 17 | 9 | 18 | — | — |
| MID. ATLANTIC | 465 | 405 | 126 | 90 | 64 | 54 | 355 | 399 | 15 | 21 |
| Upstate N.Y. | 158 | 123 | 51 | 39 | 38 | 35 | 30 | 36 | 11 | 1 |
| N.Y. City | 67 | 66 | U | U | U | U | 229 | 233 | 3 | 9 |
| N.J. | 98 | 86 | N | N | 12 | 4 | 52 | 74 | 1 | 10 |
| Pa. | 142 | 130 | 75 | 51 | 14 | 15 | 44 | 56 | — | 1 |
| E.N. CENTRAL | 404 | 543 | 305 | 270 | 97 | 95 | 223 | 363 | 17 | 25 |
| Ohio | 109 | 135 | 198 | 198 | 44 | 47 | 81 | 101 | 2 | 1 |
| Ind. | 42 | 54 | 105 | 72 | 25 | 18 | 30 | 23 | 1 | 1 |
| Ill. | 82 | 158 | 2 | — | 24 | — | 72 | 140 | 3 | 2 |
| Mich. | 163 | 155 | — | N | — | N | 32 | 83 | 9 | 21 |
| Wis. | 8 | 41 | N | N | 4 | 30 | 8 | 16 | 2 | — |
| W.N. CENTRAL | 139 | 167 | 29 | 11 | 43 | 32 | 87 | 82 | 1 | 2 |
| Minn. | 53 | 72 | — | — | 24 | 18 | 16 | 14 | — | 1 |
| Iowa | N | N | N | N | — | N | 1 | 4 | — | — |
| Mo. | 44 | 40 | 27 | 9 | 4 | 8 | 61 | 45 | 1 | 1 |
| N. Dak. | 2 | 6 | — | — | 1 | — | — | — | — | — |
| S. Dak. | 9 | 8 | 2 | 2 | — | — | — | — | — | — |
| Nebr. | 9 | 12 | — | — | 4 | 4 | 2 | 5 | — | — |
| Kans. | 22 | 29 | N | N | 10 | 2 | 7 | 14 | — | — |
| S. ATLANTIC | 425 | 459 | 502 | 596 | 43 | 28 | 722 | 754 | 20 | 26 |
| Del. | — | 2 | 1 | 3 | — | N | 6 | 3 | — | — |
| Md. | 115 | 74 | — | — | 29 | 20 | 132 | 143 | 7 | 3 |
| D.C. | 5 | 4 | 13 | 5 | 2 | 4 | 50 | 21 | — | 1 |
| Va. | 27 | 37 | N | N | — | N | 35 | 32 | 3 | 1 |
| W. Va. | 8 | 14 | 50 | 65 | 12 | 4 | 2 | 3 | — | — |
| N.C. | 68 | 65 | N | N | U | U | 97 | 64 | 5 | 1 |
| S.C. | 11 | 43 | — | 68 | — | N | 26 | 56 | — | 7 |
| Ga. | 83 | 119 | 155 | 149 | — | N | 84 | 132 | — | 1 |
| Fla. | 108 | 101 | 283 | 306 | — | N | 290 | 300 | 5 | 12 |
| E.S. CENTRAL | 79 | 121 | 88 | 77 | 3 | 9 | 153 | 158 | 11 | 7 |
| Ky. | 19 | 35 | 14 | 19 | N | N | 15 | 23 | — | — |
| Tenn. | 60 | 86 | 74 | 56 | — | N | 66 | 57 | 8 | 1 |
| Ala. | — | — | — | — | — | N | 57 | 59 | 3 | 4 |
| Miss. | — | — | — | 2 | 3 | 9 | 15 | 19 | — | 2 |
| W.S. CENTRAL | 85 | 277 | 79 | 38 | 52 | 103 | 487 | 447 | 20 | 32 |
| Ark. | 7 | 6 | 8 | 5 | 10 | 7 | 22 | 13 | — | 3 |
| La. | 5 | 1 | 71 | 33 | 17 | 20 | 107 | 103 | 2 | 2 |
| Okla. | 62 | 32 | N | N | 16 | 23 | 17 | 12 | 1 | 2 |
| Tex. | 11 | 238 | N | N | 9 | 53 | 341 | 319 | 17 | 25 |
| MOUNTAIN | 320 | 248 | 41 | 17 | 31 | 25 | 140 | 156 | 13 | 13 |
| Mont. | — | — | — | — | — | — | 5 | — | — | — |
| Idaho | 1 | 4 | N | N | — | N | 13 | 10 | 1 | 2 |
| Wyo. | 2 | 5 | 16 | 4 | — | — | — | 1 | — | — |
| Colo. | 123 | 49 | N | N | 30 | 25 | 15 | 28 | — | — |
| N. Mex. | 23 | 53 | — | 5 | — | — | 18 | 42 | 1 | 2 |
| Ariz. | 127 | 116 | N | N | — | N | 56 | 66 | 11 | 9 |
| Utah | 43 | 21 | 24 | 6 | 1 | — | 4 | 2 | — | — |
| Nev. | 1 | — | 1 | 2 | — | — | 29 | 7 | — | — |
| PACIFIC | 40 | 38 | — | 61 | — | — | 540 | 598 | 4 | 35 |
| Wash. | N | N | N | N | N | N | 60 | 33 | — | — |
| Oreg. | N | N | N | N | — | N | 12 | 14 | — | — |
| Calif. | — | — | N | N | N | N | 462 | 548 | 4 | 35 |
| Alaska | — | — | — | — | — | N | 4 | — | — | — |
| Hawaii | 40 | 38 | — | 61 | — | — | 2 | 3 | — | — |
| Guam | — | — | — | — | — | — | — | — | — | — |
| P.R. | N | N | N | N | — | N | 64 | 56 | 6 | 3 |
| V.I. | — | — | — | — | — | — | — | 4 | — | — |
| Amer. Samoa | U | U | U | U | U | U | U | U | U | U |
| C.N.M.I. | — | U | — | U | — | U | — | U | — | U |

N: Not notifiable. U: Unavailable. —: No reported cases. C.N.M.I.: Commonwealth of Northern Mariana Islands.
* Incidence data for reporting years 2004 and 2005 are provisional and cumulative (year-to-date).

**TABLE II. (*Continued*) Provisional cases of selected notifiable diseases, United States, weeks ending May 28, 2005, and May 29, 2004 (21st Week)***

| Reporting area | Tuberculosis | | Typhoid fever | | Varicella (chickenpox) | | West Nile virus disease† | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Neuroinvasive | | Non-neuroinvasive§ |
| | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 | Cum. 2004 | Cum. 2005 |
| UNITED STATES | 3,469 | 4,889 | 77 | 101 | 9,751 | 11,295 | — | 28 | — |
| NEW ENGLAND | 104 | 146 | 8 | 11 | 371 | 1,387 | — | — | — |
| Maine | 6 | 8 | — | — | 101 | 44 | — | — | — |
| N.H. | 4 | 6 | — | — | 54 | — | — | — | — |
| Vt. | — | — | — | — | 24 | 332 | — | — | — |
| Mass. | 70 | 79 | 6 | 10 | 192 | 26 | — | — | — |
| R.I. | 6 | 17 | — | 1 | — | — | — | — | — |
| Conn. | 18 | 36 | 2 | — | U | 985 | — | — | — |
| MID. ATLANTIC | 789 | 734 | 22 | 28 | 2,306 | 31 | — | 1 | — |
| Upstate N.Y. | 96 | 87 | 3 | 2 | — | — | — | — | — |
| N.Y. City | 406 | 371 | 5 | 10 | — | — | — | — | — |
| N.J. | 177 | 153 | 7 | 11 | — | — | — | — | — |
| Pa. | 110 | 123 | 7 | 5 | 2,306 | 31 | — | 1 | — |
| E.N. CENTRAL | 499 | 427 | 4 | 11 | 3,250 | 3,520 | — | — | — |
| Ohio | 99 | 73 | — | 2 | 771 | 893 | — | — | — |
| Ind. | 53 | 54 | — | — | 120 | N | — | — | — |
| Ill. | 242 | 199 | 1 | 5 | 17 | 1 | — | — | — |
| Mich. | 71 | 74 | 1 | 3 | 2,108 | 2,253 | — | — | — |
| Wis. | 34 | 27 | 2 | 1 | 234 | 373 | — | — | — |
| W.N. CENTRAL | 180 | 159 | 1 | 2 | 72 | 123 | — | 1 | — |
| Minn. | 73 | 62 | 1 | 1 | — | — | — | — | — |
| Iowa | 17 | 15 | — | — | N | N | — | — | — |
| Mo. | 47 | 47 | — | 1 | 3 | 2 | — | — | — |
| N. Dak. | 2 | 3 | — | — | 10 | 68 | — | — | — |
| S. Dak. | 5 | 4 | — | — | 59 | 53 | — | 1 | — |
| Nebr. | 15 | 6 | — | — | — | — | — | — | — |
| Kans. | 21 | 22 | — | — | — | — | — | — | N |
| S. ATLANTIC | 742 | 1,023 | 11 | 9 | 894 | 1,283 | — | 1 | — |
| Del. | 2 | 9 | — | — | 6 | 4 | — | — | — |
| Md. | 93 | 88 | 2 | 2 | — | — | — | — | — |
| D.C. | 27 | 4 | — | — | 15 | 17 | — | — | — |
| Va. | 100 | 78 | 2 | 3 | 144 | 316 | — | — | — |
| W. Va. | 8 | 10 | — | — | 552 | 680 | — | — | N |
| N.C. | 74 | 96 | 2 | 2 | — | N | — | — | — |
| S.C. | 80 | 83 | — | — | 177 | 266 | — | — | — |
| Ga. | 66 | 270 | 2 | — | — | — | — | — | — |
| Fla. | 292 | 385 | 3 | 2 | — | — | — | 1 | — |
| E.S. CENTRAL | 201 | 178 | 1 | 4 | — | — | — | — | — |
| Ky. | 40 | 31 | 1 | 2 | N | N | — | — | — |
| Tenn. | 95 | 48 | — | 2 | — | — | — | — | — |
| Ala. | 66 | 66 | — | — | — | — | — | — | — |
| Miss. | — | 33 | — | — | — | — | — | — | — |
| W.S. CENTRAL | 278 | 861 | 3 | 9 | 1,349 | 3,509 | — | 2 | — |
| Ark. | 36 | 55 | — | — | — | — | — | — | — |
| La. | — | — | — | — | 97 | 42 | — | — | — |
| Okla. | 54 | 60 | — | — | — | — | — | — | — |
| Tex. | 188 | 746 | 3 | 9 | 1,252 | 3,467 | — | 2 | — |
| MOUNTAIN | 86 | 206 | 3 | 3 | 1,509 | 1,442 | — | 23 | — |
| Mont. | — | — | — | — | — | — | — | — | — |
| Idaho | — | — | — | — | — | — | — | — | — |
| Wyo. | — | 1 | — | — | 42 | 18 | — | — | — |
| Colo. | 16 | 52 | — | 1 | 1,081 | 1,080 | — | 1 | — |
| N. Mex. | 4 | 14 | — | — | 78 | 65 | — | — | — |
| Ariz. | 56 | 83 | 1 | 1 | — | — | — | 22 | — |
| Utah | 10 | 18 | 1 | 1 | 308 | 279 | — | — | — |
| Nev. | — | 38 | 1 | — | — | — | — | — | — |
| PACIFIC | 590 | 1,155 | 24 | 24 | — | — | — | — | — |
| Wash. | 86 | 81 | 1 | 1 | N | N | — | — | — |
| Oreg. | 38 | 36 | 2 | — | — | — | — | — | — |
| Calif. | 406 | 981 | 17 | 17 | — | — | — | — | — |
| Alaska | 13 | 12 | — | — | — | — | — | — | — |
| Hawaii | 47 | 45 | 4 | 6 | — | — | — | — | — |
| Guam | — | 14 | — | — | — | 99 | — | — | — |
| P.R. | — | 21 | — | — | 76 | 147 | — | — | — |
| V.I. | — | — | — | — | — | — | — | — | — |
| Amer. Samoa | U | U | U | U | U | U | U | U | — |
| C.N.M.I. | — | U | — | U | — | U | — | U | — |

N: Not notifiable. U: Unavailable. —: No reported cases. C.N.M.I.: Commonwealth of Northern Mariana Islands.

* Incidence data for reporting years 2004 and 2005 are provisional and cumulative (year-to-date).

† Updated weekly from reports to the Division of Vector-Borne Infectious Diseases, National Center for Infectious Diseases (ArboNet Surveillance).

§ Not previously notifiable.

**TABLE III. Deaths in 122 U.S. cities,* week ending May 28, 2005 (21st Week)**

| Reporting Area | All causes, by age (years) | | | | | | P&I† Total |
|---|---|---|---|---|---|---|---|
| | All Ages | ≥65 | 45–64 | 25–44 | 1–24 | <1 | |
| NEW ENGLAND | 440 | 315 | 89 | 23 | 7 | 6 | 46 |
| Boston, Mass. | 119 | 77 | 30 | 8 | 1 | 3 | 15 |
| Bridgeport, Conn. | 30 | 27 | 2 | — | 1 | — | 3 |
| Cambridge, Mass. | 12 | 8 | 4 | — | — | — | 1 |
| Fall River, Mass. | 21 | 17 | 3 | 1 | — | — | 1 |
| Hartford, Conn. | 52 | 34 | 10 | 4 | 3 | 1 | 7 |
| Lowell, Mass. | 11 | 8 | 3 | — | — | — | — |
| Lynn, Mass. | 11 | 7 | 4 | — | — | — | 1 |
| New Bedford, Mass. | 23 | 18 | 3 | 2 | — | — | 1 |
| New Haven, Conn. | 31 | 19 | 9 | 2 | 1 | — | 4 |
| Providence, R.I. | U | U | U | U | U | U | U |
| Somerville, Mass. | 4 | 4 | — | — | — | — | — |
| Springfield, Mass. | 38 | 28 | 7 | 1 | — | 2 | 4 |
| Waterbury, Conn. | 31 | 23 | 5 | 3 | — | — | 1 |
| Worcester, Mass. | 57 | 45 | 9 | 2 | 1 | — | 8 |
| MID. ATLANTIC | 2,084 | 1,405 | 459 | 128 | 56 | 36 | 109 |
| Albany, N.Y. | 46 | 26 | 12 | 5 | 1 | 2 | 1 |
| Allentown, Pa. | 28 | 25 | 1 | 2 | — | — | 2 |
| Buffalo, N.Y. | 68 | 37 | 19 | 4 | 4 | 4 | 4 |
| Camden, N.J. | 25 | 17 | 5 | 2 | — | 1 | 1 |
| Elizabeth, N.J. | 16 | 14 | 1 | 1 | — | — | 3 |
| Erie, Pa. | 50 | 41 | 7 | 1 | — | 1 | 4 |
| Jersey City, N.J. | 34 | 21 | 9 | 3 | — | 1 | — |
| New York City, N.Y. | 1,109 | 752 | 254 | 65 | 24 | 14 | 54 |
| Newark, N.J. | 64 | 32 | 18 | 6 | 6 | 2 | — |
| Paterson, N.J. | 5 | 2 | 3 | — | — | — | — |
| Philadelphia, Pa. | 246 | 147 | 59 | 22 | 13 | 5 | 15 |
| Pittsburgh, Pa.§ | 15 | 6 | 5 | — | — | 4 | — |
| Reading, Pa. | 20 | 14 | 5 | 1 | — | — | 3 |
| Rochester, N.Y. | 148 | 108 | 30 | 7 | 2 | 1 | 5 |
| Schenectady, N.Y. | 21 | 16 | 4 | 1 | — | — | 4 |
| Scranton, Pa. | 41 | 36 | 4 | 1 | — | — | 2 |
| Syracuse, N.Y. | 89 | 67 | 15 | 5 | 2 | — | 10 |
| Trenton, N.J. | 22 | 12 | 5 | 1 | 3 | 1 | — |
| Utica, N.Y. | 17 | 14 | 2 | 1 | — | — | 1 |
| Yonkers, N.Y. | 20 | 18 | 1 | — | 1 | — | — |
| E.N. CENTRAL | 1,987 | 1,276 | 475 | 138 | 46 | 52 | 130 |
| Akron, Ohio | 53 | 35 | 10 | 2 | 2 | 4 | 4 |
| Canton, Ohio | 37 | 27 | 10 | — | — | — | 4 |
| Chicago, Ill. | 335 | 192 | 83 | 35 | 13 | 12 | 20 |
| Cincinnati, Ohio | 105 | 61 | 27 | 9 | 5 | 3 | 6 |
| Cleveland, Ohio | 258 | 180 | 51 | 17 | 2 | 8 | 6 |
| Columbus, Ohio | 172 | 96 | 53 | 16 | 3 | 4 | 13 |
| Dayton, Ohio | 118 | 79 | 27 | 5 | 2 | 5 | 8 |
| Detroit, Mich. | 184 | 96 | 61 | 16 | 4 | 7 | 10 |
| Evansville, Ind. | 54 | 37 | 11 | 4 | 2 | — | 4 |
| Fort Wayne, Ind. | 47 | 36 | 8 | 3 | — | — | 4 |
| Gary, Ind. | 6 | 3 | 2 | — | — | 1 | 1 |
| Grand Rapids, Mich. | 60 | 49 | 10 | 1 | — | — | 3 |
| Indianapolis, Ind. | 121 | 81 | 30 | 4 | 4 | 2 | 12 |
| Lansing, Mich. | 55 | 42 | 8 | 3 | 1 | 1 | 4 |
| Milwaukee, Wis. | 111 | 68 | 30 | 9 | 2 | 2 | 8 |
| Peoria, Ill. | 56 | 42 | 5 | 4 | 4 | 1 | 6 |
| Rockford, Ill. | 58 | 43 | 11 | 4 | — | — | 2 |
| South Bend, Ind. | 61 | 46 | 12 | 2 | — | 1 | 6 |
| Toledo, Ohio | 96 | 63 | 26 | 4 | 2 | 1 | 9 |
| Youngstown, Ohio | U | U | U | U | U | U | U |
| W.N. CENTRAL | 652 | 414 | 144 | 51 | 22 | 20 | 40 |
| Des Moines, Iowa | 60 | 45 | 9 | 3 | 3 | — | 4 |
| Duluth, Minn. | 25 | 21 | 3 | — | — | 1 | 3 |
| Kansas City, Kans. | 36 | 24 | 6 | 4 | — | 2 | — |
| Kansas City, Mo. | 88 | 52 | 22 | 6 | 5 | 3 | 3 |
| Lincoln, Nebr. | 38 | 34 | 3 | — | — | 1 | 1 |
| Minneapolis, Minn. | 57 | 25 | 18 | 8 | 3 | 3 | 8 |
| Omaha, Nebr. | 73 | 57 | 9 | 5 | — | 2 | 4 |
| St. Louis, Mo. | 124 | 64 | 31 | 16 | 8 | 4 | 12 |
| St. Paul, Minn. | 61 | 36 | 19 | 2 | 2 | 2 | 4 |
| Wichita, Kans. | 90 | 56 | 24 | 7 | 1 | 2 | 1 |
| S. ATLANTIC | 1,204 | 733 | 315 | 82 | 40 | 34 | 67 |
| Atlanta, Ga. | 111 | 54 | 31 | 10 | 2 | 14 | 5 |
| Baltimore, Md. | 189 | 111 | 45 | 16 | 12 | 5 | 15 |
| Charlotte, N.C. | 125 | 77 | 35 | 6 | 3 | 4 | 8 |
| Jacksonville, Fla. | 116 | 68 | 37 | 9 | 1 | 1 | 6 |
| Miami, Fla. | 111 | 71 | 28 | 8 | 4 | — | 9 |
| Norfolk, Va. | 53 | 35 | 14 | 3 | — | 1 | 1 |
| Richmond, Va. | 72 | 39 | 23 | 6 | 3 | 1 | 2 |
| Savannah, Ga. | 59 | 40 | 15 | 2 | 2 | — | 2 |
| St. Petersburg, Fla. | 58 | 46 | 5 | 1 | 5 | 1 | 6 |
| Tampa, Fla. | 195 | 128 | 49 | 10 | 2 | 6 | 10 |
| Washington, D.C. | 99 | 54 | 28 | 10 | 6 | 1 | 2 |
| Wilmington, Del. | 16 | 10 | 5 | 1 | — | — | 1 |
| E.S. CENTRAL | 801 | 534 | 182 | 51 | 18 | 16 | 57 |
| Birmingham, Ala. | 167 | 117 | 36 | 7 | 3 | 4 | 18 |
| Chattanooga, Tenn. | 75 | 45 | 19 | 6 | 4 | 1 | 2 |
| Knoxville, Tenn. | 73 | 54 | 13 | 5 | — | 1 | 7 |
| Lexington, Ky. | 67 | 42 | 17 | 4 | 3 | 1 | 4 |
| Memphis, Tenn. | 157 | 99 | 38 | 13 | 4 | 3 | 5 |
| Mobile, Ala. | 60 | 40 | 15 | 3 | 1 | 1 | 3 |
| Montgomery, Ala. | 58 | 38 | 12 | 7 | — | 1 | 7 |
| Nashville, Tenn. | 144 | 99 | 32 | 6 | 3 | 4 | 11 |
| W.S. CENTRAL | 1,508 | 968 | 349 | 100 | 53 | 38 | 74 |
| Austin, Tex. | 88 | 52 | 26 | 5 | 3 | 2 | 11 |
| Baton Rouge, La. | 28 | 19 | 7 | 1 | 1 | — | — |
| Corpus Christi, Tex. | 44 | 34 | 8 | — | 1 | 1 | 2 |
| Dallas, Tex. | 208 | 125 | 55 | 16 | 9 | 3 | 18 |
| El Paso, Tex. | 88 | 62 | 16 | 4 | 4 | 2 | 5 |
| Ft. Worth, Tex. | 133 | 86 | 26 | 12 | 3 | 6 | 3 |
| Houston, Tex. | 365 | 216 | 95 | 31 | 12 | 11 | 21 |
| Little Rock, Ark. | 76 | 48 | 19 | 4 | 3 | 2 | — |
| New Orleans, La. | 30 | 11 | 13 | 2 | 1 | 3 | 1 |
| San Antonio, Tex. | 242 | 166 | 46 | 13 | 11 | 6 | 12 |
| Shreveport, La. | 43 | 34 | 7 | 1 | 1 | — | 1 |
| Tulsa, Okla. | 163 | 115 | 31 | 11 | 4 | 2 | — |
| MOUNTAIN | 1,131 | 739 | 244 | 87 | 31 | 27 | 68 |
| Albuquerque, N.M. | 137 | 85 | 29 | 16 | 6 | 1 | 12 |
| Boise, Idaho | 34 | 23 | 4 | 3 | — | 4 | 2 |
| Colo. Springs, Colo. | 64 | 43 | 15 | 3 | 2 | 1 | 5 |
| Denver, Colo. | 101 | 62 | 16 | 13 | 2 | 8 | 6 |
| Las Vegas, Nev. | 265 | 166 | 66 | 21 | 8 | 3 | 15 |
| Ogden, Utah | 32 | 25 | 4 | 2 | 1 | — | — |
| Phoenix, Ariz. | 184 | 112 | 49 | 12 | 5 | 4 | 8 |
| Pueblo, Colo. | 41 | 29 | 10 | 1 | 1 | — | 2 |
| Salt Lake City, Utah | 97 | 60 | 18 | 11 | 3 | 5 | 7 |
| Tucson, Ariz. | 176 | 134 | 33 | 5 | 3 | 1 | 11 |
| PACIFIC | 1,755 | 1,237 | 372 | 92 | 29 | 25 | 158 |
| Berkeley, Calif. | 16 | 12 | 3 | 1 | — | — | 1 |
| Fresno, Calif. | 179 | 133 | 33 | 7 | 4 | 2 | 14 |
| Glendale, Calif. | 19 | 16 | 3 | — | — | — | 2 |
| Honolulu, Hawaii | 93 | 71 | 18 | 4 | — | — | 6 |
| Long Beach, Calif. | 73 | 47 | 19 | 7 | — | — | 6 |
| Los Angeles, Calif. | 267 | 191 | 46 | 19 | 7 | 4 | 31 |
| Pasadena, Calif. | 44 | 30 | 12 | 1 | 1 | — | 8 |
| Portland, Oreg. | 119 | 80 | 28 | 5 | 3 | 3 | 6 |
| Sacramento, Calif. | 161 | 110 | 40 | 8 | — | 3 | 19 |
| San Diego, Calif. | 145 | 112 | 27 | 4 | 2 | — | 6 |
| San Francisco, Calif. | 173 | 117 | 36 | 13 | 3 | 4 | 19 |
| San Jose, Calif. | 178 | 129 | 32 | 9 | 7 | 1 | 18 |
| Santa Cruz, Calif. | 28 | 18 | 8 | 2 | — | — | 3 |
| Seattle, Wash. | 108 | 63 | 33 | 7 | 1 | 4 | 3 |
| Spokane, Wash. | 51 | 36 | 10 | 1 | 1 | 3 | 6 |
| Tacoma, Wash. | 101 | 72 | 24 | 4 | — | 1 | 10 |
| TOTAL | 11,562¶ | 7,621 | 2,629 | 752 | 302 | 254 | 749 |

U: Unavailable. —: No reported cases.

* Mortality data in this table are voluntarily reported from 122 cities in the United States, most of which have populations of ≥100,000. A death is reported by the place of its occurrence and by the week that the death certificate was filed. Fetal deaths are not included.

† Pneumonia and influenza.

§ Because of changes in reporting methods in this Pennsylvania city, these numbers are partial counts for the current week. Complete counts will be available in 4 to 6 weeks.

¶ Total includes unknown ages.

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# A Human-Health Risk Assessment for West Nile Virus and Insecticides Used in Mosquito Management

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**West Nile virus (WNV) has been a major public health concern in North America since 1999, when the first outbreak in the Western Hemisphere occurred in New York City. As a result of this ongoing disease outbreak, management of mosquitoes that vector WNV throughout the United States and Canada has necessitated using insecticides in areas where they traditionally have not been used or have been used less frequently. This has resulted in concerns by the public about the risks from insecticide use. The objective of this study was to use reasonable worst-case risk assessment methodologies to evaluate human-health risks for WNV and the insecticides most commonly used to control adult mosquitoes. We evaluated documented health effects from WNV infection and determined potential population risks based on reported frequencies. We determined potential acute (1-day) and subchronic (90-day) multiroute residential exposures from each insecticide for several human subgroups during a WNV disease outbreak scenario. We then compared potential insecticide exposures to toxicologic and regulatory effect levels. Risk quotients (RQs, the ratio of exposure to toxicologic effect) were < 1.0 for all subgroups. Acute RQs ranged from 0.0004 to 0.4726, and subchronic RQs ranged from 0.00014 to 0.2074. Results from our risk assessment and the current weight of scientific evidence indicate that human-health risks from residential exposure to mosquito insecticides are low and are not likely to exceed levels of concern. Further, our results indicate that, based on human-health criteria, the risks from WNV exceed the risks from exposure to mosquito insecticides.**
***Key words:*** **comparative risk assessment, mosquito control, organophosphates, pesticide exposure, pyrethroids, risk analysis, vectorborne disease.** ***Environ Health Perspect*** **114:366–372 (2006). doi:10.1289/ehp.8667 available via *http://dx.doi.org/* [Online 28 October 2005]**

West Nile virus (WNV) has become a major public health concern in North America since 1999, when the first outbreak in the Western Hemisphere occurred in New York City, causing 62 cases of human encephalitis and 7 deaths [Centers for Disease Control and Prevention (CDC) 1999]. The initial outbreak in New York City is thought to have affected 2.6% of the population (Hubalek 2001). In 2000, WNV spread to three states, with 21 human cases of WNV infection and 2 deaths. In 2001, 66 human cases and 9 deaths were reported in 10 states, before WNV spread westward, affecting all but 6 states in 2002 and causing the largest arboviral encephalitis epidemic in U.S. history (Huhn et al. 2003). A total of 4,156 human cases were documented, with 284 deaths reported (CDC 2003), and numbers continued to grow in 2003, when 46 states reported 9,862 human cases with 264 deaths (CDC 2004a). In 2004, 2,539 human cases and 100 deaths were reported in 41 states (Hayes et al. 2005). Since the first appearance of WNV in the United States in 1999, the CDC has reported 16,706 documented human cases and 666 deaths (CDC 2004b; Hayes et al. 2005); however, large numbers of human infections may not be detected because of significant underreporting of milder cases of West Nile fever (Hubalek 2001; Huhn et al. 2003). Given the infection rate observed for previous years, Peleman (2004) estimated that 1.5 million people were infected with the virus in 2003.

As a result of this ongoing disease outbreak, management of mosquitoes that vector WNV throughout the United States and Canada has necessitated using insecticides in areas where they traditionally have not been used or have been used less frequently. This practice has raised concerns by the public about risks from insecticide use. In a survey by Hinten (2000), 54% of 880 people surveyed were either equally afraid of WNV and pesticides or were more afraid of the insecticides. Since 1999, numerous concerns have been raised by the public regarding the safety of using insecticides to control mosquitoes (Cohen 2003; Fehr-Snyder 2004; Fitz 2003). Some of those concerned have even suggested that the health risks from the insecticides exceed those of WNV (Cohen 2003; Ziem 2005). These concerns by the public are not exclusive to the WNV issue, but reflect long-standing perceptions of risk from pesticides (Peterson and Higley 1993; Slovic 1987).

Risk assessment is a formalized basis for the objective evaluation of risk in which assumptions and uncertainties are clearly considered and presented [National Research Council (NRC) 1983, 1996]. Human-health and ecologic risk can be described in quantitative terms as a function of effect (also termed "hazard" or "toxicity") and exposure (NRC 1983). Risk assessment typically uses a tiered modeling approach extending from deterministic models (tier 1) based on conservative assumptions to probabilistic models (tier 4) using refined assumptions [Society for Environmental Toxicology and Chemistry (SETAC) 1994]. In risk assessment, conservative assumptions in lower-tier assessments represent overestimates of effect and exposure; therefore, the resulting quantitative risk values typically are conservative and err on the side of safety.

Unfortunately, few, if any, science-based considerations of the risks of insecticide use versus the risks from vectorborne diseases have been examined. An understanding of the human-health risks for both vectorborne diseases and associated vector controls would aid greatly in decision making by all stakeholders. Therefore, the objective of this study was to use risk assessment methodologies to evaluate human-health risks from WNV and from the insecticides used to control adult mosquitoes.

## Materials and Methods

***Problem formulation.*** Although WNV has important effects on horses and birds, our assessment of health risks from WNV focused only on humans. Currently, effect and exposure factors for WNV are poorly understood (Loeb et al. 2005), making quantitative modeling of risk difficult. Therefore, we evaluated documented health effects from WNV infection and determined potential population risks based on reported frequencies. Because of the relatively recent emergence of WNV in North America, information on prevalence of various effects of the disease should be regarded as tentative.

Our tier-1 quantitative assessment of human-health risks associated with insecticides

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used in mosquito control focused on acute and subchronic residential exposures after truck-mounted ultra-low-volume (ULV) spraying of mosquito adulticides. The dissemination of mosquito adulticides by ULV application generates fine aerosol droplets that remain aloft and target flying mosquitoes [U.S. Environmental Protection Agency (EPA) 2002b]. Acute exposures were defined as single-day exposures immediately after a spray event. Subchronic exposures were defined as exposures per day over a 90-day seasonal multispray event. A total of 10 spray events were assumed to occur on days 1, 4, 14, 17, 27, 30, 40, 43, 53, and 56. This design represents a reasonable worst-case mosquito insecticide seasonal application scenario, including during a human epidemic of WNV [Karpati et al. 2004; New York City Department of Health (NYCDOH) 2001]. Chronic exposures (> 6 months) to mosquito adulticides are unlikely. Additionally, extrapolation of subchronic exposures to chronic exposure time frames would result in lower risks than with subchronic risks (NYCDOH 2001). Therefore, chronic risks were not assessed in this study.

Exposures to several population subgroups were estimated to account for potential age-related differences in exposure. Groups included adult males, adult females, infants (0.5–1.5 years of age), and children (2–3, 5–6, and 10–12 years of age). Adult males were assumed to weigh 71.8 kg, which represents the mean body weight for all males > 18 years of age, and adult reproductive females were assumed to weigh 60 kg, which represents the mean body weight for females between 13 and 54 years of age (U.S. EPA 1996). Children 5–6 and 10–12 years of age were assumed to weigh 21.1 and 40.9 kg, respectively. Infants (0.5–1.5 years of age) and toddlers (2–3 years of age) were assumed to weigh 9.4 and 14.3 kg, respectively. All weights for children were derived from mean body weight values for male and female children within their respective age groups (U.S. EPA 1996).

***Hazard identification.*** We conducted human-health risk assessments for six insecticide active ingredients (permethrin, pyrethrins, resmethrin, phenothrin, malathion, and naled) and one synergist (piperonyl butoxide). Malathion and naled are in the organophosphate class of insecticides, and permethrin, pyrethrins, resmethrin, and phenothrin are in the pyrethroid class. The synergist, piperonyl butoxide, is present in many formulations with pyrethroids. All compounds are currently registered by the U.S. EPA for adult mosquito management in the United States.

**Toxicity end points.** Toxicity and dose–response information for each compound were reviewed for acute and subchronic exposure durations. Toxicity end points in this assessment were chosen based on U.S. EPA regulatory end points.We used inhalation, dermal, and ingestion toxicity end points for each respective exposure route and duration. Ingestion reference doses (RfDs) were used as the toxicity end points (acceptable daily exposures) and were compared with total estimated exposures (total body burden). Acute and subchronic ingestion RfDs were calculated by dividing the most sensitive toxic effect [typically the no observed adverse effect level (NOAEL)] by a series of uncertainty factors (typically a factor of 100 to account for intraspecies and interspecies uncertainty) (Table 1).

***Environmental concentrations and fate of insecticides.*** We used the AERMOD, version 1.0 tier 1 air dispersion model (U.S. EPA 1999) to predict the 7.6 m (25 ft) and 91.4 m (300 ft) air concentrations (micrograms per cubic meter) of each insecticide within 1- and 6-hr time ranges after ULV application by a truck-mounted sprayer. Estimates of environmental concentrations are presented only for truck-mounted ULV applications because our modeling suggested that delivery of ULV applications by aircraft resulted in substantially less aerial and surface deposition (and therefore less human exposure and risk). This was also observed by the NYCDOH (2001).

We used the following conservative assumptions: *a*) each chemical had a 24-hr half-life in air except for naled, which was given a 18-hr half-life; *b*) the insecticides were applied at the maximum application rate as stated on each label; *c*) all of the insecticides were susceptible to the same weather conditions using standardized weather data from Albany, New York, in 1988; *d*) all spray events occurred at 2100 hr; and *e*) each spray release was at 1.5 m. The chemical properties, application rates, and predicted environmental concentrations for each active ingredient are listed in Table 2.

Receptors were established within the model on a Cartesian grid at five intervals of

**Table 1.** Toxicologic effects and regulatory end points for the active ingredients.

| Compound | Acute | | Subchronic | |
|---|---|---|---|---|
| | End point | Study and toxicologic effects | End point | Study and toxicologic effects |
| Malathion | NOAEL = 50 mg/kg/day[a]<br>RfD = 0.5 mg/kg/day<br>UF = 100 | Based on reduction in maternal bw gain in a study with pregnant rabbits[a] | NOAEL = 2.4 mg/kg/day[a]<br>RfD = 0.024 mg/kg/day<br>UF = 100 | Based on inhibition of blood enzyme activity at 50 ppm malathion in the diet in a 24-month study in rats[a] |
| Naled | NOAEL = 1.0 mg/kg/day[b]<br>RfD = 0.01 mg/kg/day<br>UF = 100 | Based on inhibition of blood and brain enzymes in a 28-day study in rats[b] | NOAEL = 1.0 mg/kg/day[b]<br>RfD = 0.01 mg/kg/day<br>UF = 100 | Based on inhibition of blood and brain enzymes in a 28-day study in rats[b] |
| Permethrin | NOAEL = 25 mg/kg/day[c]<br>RfD = 0.25 mg/kg/day<br>UF = 100 | Acute neurotoxicity study in rats<br>LOEL = 75 mg/kg based on observations of clinical signs such as aggression, abnormal/decreased movement, and increased body temperature[c] | NOAEL = 25 mg/kg/day[c]<br>RfD = 0.25 mg/kg/day<br>UF = 100 | Acute neurotoxicity study in rats<br>LOEL = 75 mg/kg based on observations of clinical signs such as aggression, abnormal/decreased movement, and increased body temperature[c] |
| Resmethrin | NOEL = 10 mg/kg/day[d]<br>RfD = 0.1 mg/kg/day<br>UF = 100 | Based on liver weight increases in a 6-month study in dogs[d] | NOEL = 10 mg/kg/day[d]<br>RfD = 0.1 mg/kg/day<br>UF = 100 | Based on liver weight increases in a 6-month study in dogs[d] |
| Phenothrin | NOEL = 70 mg/kg/day[e]<br>RfD = 0.7 mg/kg/day<br>UF = 100 | 13-week study in rats<br>LOEL = 216 mg/kg-day based on increases in liver weights and decreases in cholesterol in both male and female rats[e] | NOEL = 70 mg/kg/day[e]<br>RfD = 0.7 mg/kg/day<br>UF = 100 | 13-week study in rats<br>LOEL = 216 mg/kg-day based on increases in liver weights and decreases in cholesterol in both male and female rats[e] |
| Pyrethrins | NOAEL = 20 mg/kg/day[f]<br>RfD = 0.07 mg/kg/day<br>UF = 300 | Acute neurotoxicity study in rats<br>LOAEL = 63 mg/kg/day based on tremors in females[f] | NOAEL = 4.37 mg/kg/day[f]<br>RfD = 0.044 mg/kg/day<br>UF = 100 | Rat chronic toxicity study<br>LOAEL = 42.9 mg/kg/day based on increased incidence of thyroid follicular cell hyperplasia in males.[f] |
| Piperonyl butoxide | NOAEL = 630 mg/kg/day[g]<br>RfD = 6.3 mg/kg/day<br>UF = 100 | Developmental toxicity study in rats<br>LOAEL = 1,065 mg/kg/day based on decreases in maternal bw gain[g] | NOAEL = 89 mg/kg/day[g]<br>RfD = 0.89 mg/kg/day<br>UF = 100 | Two generation reproduction study in rats<br>LOAEL = 469 mg/kg/day based on decrease in bw gain of $F_1$ and $F_2$ pups at postnatal day 2[g] |

Abbreviations: bw, body weight; LOAEL, lowest observed adverse effect level. LOEL, lowest observed effect level; NOEL, no observed effect level; UF, uncertainty factor used to determine the RfD.
[a]U.S. EPA 2000c. [b]U.S. EPA 2002a. [c]U.S. EPA 2005c. [d]U.S. EPA 2000a. [e]U.S. EPA 2000b. [f]U.S. EPA 2005b. [g]U.S. EPA 2005a.

25 m at 7.6 m and 91.4 m from the edge of the spray emission area. The receptors were at a height of 1.5 m. Each receptor estimated the 1- and 6-hr average air concentrations for each insecticide. An average was then taken of the estimates from the six receptors at 7.6 m that were not at the edges of the spray zone. The following data were obtained using this network of receptors: the 1-hr average concentration at 7.6 m, the 6-hr average at 7.6 m, and the peak value at 91.4 m.

We used the screening Industrial Source Complex Short-Term (ISCST3) model (U.S. EPA 1995) to estimate particle deposition (milligrams per square meter) at 7.6 m and 91.4 m from the spray area at a 1-hr average. The following assumptions were made in addition to those from AERMOD: *a*) all of the insecticides were susceptible to the same weather conditions using standardized weather data from Salem, Massachusetts; *b*) the ULV particle size applications had 3% of the emitted particles greater than the allowable particle size as stated on the label; and *c*) the particles were assigned a density in accordance with the specific gravity of each insecticide.

A Cartesian grid was used for ISCST3 that was similar to that used in AERMOD. Receptors were added at 15.24-m intervals between 7.6 m and 91.4 m from the spray source to obtain a more accurate estimate of the average deposition within 91.4 m of the source. The receptors were also at the same height of 1.5 m. All of the same methods were used to calculate the average deposition at 7.6 m and 91.4 m. The middle receptors were included to calculate an average deposition within 91.4 m. The following data were obtained from this information: deposition at 7.6 m, deposition at 91.4 m, and the average deposition within 91.4 m of the spray source.

For estimating subchronic exposures, we used the estimated deposition values within 91.4 m for each insecticide in an exponential decay model to characterize their persistence on surfaces such as soil within a spray program that included 10 sprays on days 1, 4, 14, 17, 27, 30, 40, 43, 53, and 56. Insecticide concentrations for each spray event were followed through day 90 using the following multiple degradation model:

$$D = \sum_{j=i}^{90} P e^{(r_1+r_2)t}, \qquad [1]$$

where $D$ is the sum of the deposition over one spray, $P$ is the peak deposition after a spray event, $r_1$ is the rate of decay calculated by using the aerobic soil half-life of each active ingredient, $r_2$ is the rate of decay calculated by using the soil photolysis half-life of each active ingredient, $t$ is the time in hours, and $j$ is the spray day. The average daily exposure was then determined by dividing the deposition sum by 90.

The same deposition and degradation model was used to characterize deposition and persistence on garden produce by using a Kenaga nomogram to estimate the deposition (milligrams per kilogram dry weight) of each insecticide on respective plant parts. Because the nomogram represents a linear relationship between application rate and maximum residues, it can be used to estimate the maximum residues on plant surfaces for a given application rate (Fletcher et al. 1994). For this analysis, maximum application rates were used for each insecticide, and each estimated concentration was then applied to the model above, using the surface photolysis half-life to estimate the rate of degradation.

***Acute exposure.*** We assumed that multiroute exposures immediately after a single-spray event were limited to 24 hr. Routes of insecticide exposure included inhalation, dermal contact with spray, hand-to-mouth ingestion by infants and toddlers from spray deposition on hands, and ingestion of garden produce. We also assumed that residents did nothing to limit their exposure to the spray. In its assessment of acute and subchronic exposures from several mosquito adulticides, the NYCDOH (2001) concluded that exposures from potable water and swimming were negligible. Using environmental fate models, we also concluded that the chemical properties of the insecticides result in negligible concentrations in water. Therefore, we did not include these exposures in our assessment.

**Acute inhalation exposure.** Acute inhalation exposures were estimated as

$$PE = (EEC \times RR \times D \times CF) \div bw, \qquad [2]$$

where $PE$ is potential exposure [milligrams per kilogram body weight (bw)], $EEC$ is the 6-hr average estimated environmental concentration of an active ingredient in the air 1.5 m high at 7.6 m from the spray source (micrograms per cubic meter), $RR$ is the respiratory rate under moderate activity (cubic meters per hour), $D$ is the duration of exposure (hours), $CF$ is the conversion factor to account for the conversion of units from micrograms per cubic meter to milligrams per cubic meter, and $bw$ is body weight (kilograms).

RRs were assumed to be 1.6 $m^3$/hr for adults and 1.2 $m^3$/hr for children, including infants. These rates are indicative of moderate physical activity (U.S. EPA 1996). The duration of exposure was 6 hr. Therefore, the assumption was that the person was outside and 7.6 m from the spray truck when it passed him or her. Moreover, the person remained outside, 7.6 m from the emission, for the following 6 hr, respiring as if under moderate physical activity during the entire time. Body weight for the different age groups is discussed above.

**Acute dermal exposure from spray deposition.** Acute dermal exposures from deposition of spray drift on skin were estimated as

$$PE = (TDE \times AB) \div bw, \qquad [3]$$

where $PE$ is potential exposure (milligrams per kilogram bw), $TDE$ is total dermal exposure (milligrams), $AB$ is dermal absorption rate, and $bw$ is body weight (kilograms). There is no publicly available information on dermal deposition immediately after truck-mounted ULV sprays. Therefore, we used the U.S. EPA Pesticide Handler Exposure Database (PHED; U.S. EPA 1998) as a conservative surrogate. The PHED contains pesticide-handler scenarios derived from field studies and exposure estimates based on physical factors such as application rate, hectares treated per day, type of clothing worn, methods of application, and

**Table 2.** Application rates, chemical properties, and predicted environmental concentrations of active ingredients.

| Property | Active ingredient | | | | | | |
|---|---|---|---|---|---|---|---|
| | Piperonyl butoxide | Phenothrin | Permethrin | Resmethrin | Malathion | Naled | Pyrethrins |
| Application rate (kg ai/ha) | 0.0392 | 0.004 | 0.0078 | 0.0078 | 0.0639 | 0.0224 | 0.009 |
| Density (g/mL) | 0.898[a] | 0.898[a] | 0.8657[b] | 0.87[c] | 1.23[d] | 1.67[e] | 0.81[f] |
| Surface photolysis half-life (days) | NA[g] | 6[c] | 23[h] | 0.14[i] | 6.5[i] | 2.4[i] | 0.5[j] |
| Soil aerobic half-life (days) | 14[i] | 7[i] | 37[k] | 30[h] | 1[h] | 1[h] | 1[j] |
| Acute air concentration (μg/$m^3$)[l] | 7.39 | 0.81 | 1.55 | 1.61 | 9.76 | 1.68 | 1.7 |
| 1-Day acute produce concentration (mg/kg dry wt) | 0.525 | 0.054 | 0.105 | 0.105 | 0.855 | 0.3 | 0.12 |
| 90-Day mean surface concentration (mg/$m^2$)[m] | 15.42 | 0.43 | 4.14 | 0.22 | 2.18 | 0.65 | 0.54 |
| 90-Day mean produce concentration (mg/kg dry wt) | 2.88 | 0.055 | 0.096 | 0.012 | 0.73 | 0.13 | 0.21 |

Abbreviations: ai/ha, active ingredient per hectare; NA, not available; wt, weight.
[a]Clarke Mosquito Control Products (1999b). [b]Clarke Mosquito Control Products (1999a). [c]Bayer Environmental Science (2004). [d]Griffin (2001). [e]AMVAC (2003). [f]McLaughlin Gormley King Co. (2004). [g]Surface and produce concentrations determined from soil aerobic half-life only. [h]U.S. Department of Agriculture (USDA 2005). [i]NYCDOH (2001). [j]Food and Agricultural Organization (2000). [k]U.S. EPA (2005c). [l]6-Hr mean concentration at 7.6 m from spray source. [m]90-Day mean surface concentration within 91.4 m of the spray source.

formulation type. We used the PHED scenario in which a flagger (person marking the location for pesticide application while the application is occurring) was exposed to a liquid application. We assumed that the person was not wearing clothing and that the exposure was 10 times greater than the flagger scenario. We believe this scenario conservatively estimated residential dermal exposure for two reasons: *a*) we added a 10-fold increase in exposure, and *b*) the U.S. EPA has not considered acute dermal contact from ULV applications for pyrethrins, piperonyl butoxide, and permethrin because it was believed to be negligible (U.S. EPA 2005a, 2005b, 2005c). The values for percent dermal absorption were 0.22% for pyrethrins (U.S. EPA 2005b), 2% for piperonyl butoxide (U.S. EPA 2005a), 10% for malathion and resmethrin (U.S. EPA 2000a, 2000c), 15% for permethrin (U.S. EPA 2005c), 70% for phenothrin (U.S. EPA 2000b), and 100% for naled (U.S. EPA 2002a).

**Acute hand-to-mouth exposure from spray deposition on hands.** Acute hand-to-mouth exposures were estimated for only two subgroups (toddlers and infants), because young children are more likely than adults to be exposed to pesticides as a result of hand-to-mouth contact (Cohen Hubal et al. 2000). Exposures were calculated as

$$PE = [(THD \div HSA) \times AHS \times SEF] \div bw, \quad [4]$$

where *PE* is potential exposure (milligrams per kilogram bw), *THD* is total hand dermal exposure (milligrams), *HSA* is adult hand surface area (square meters), *AHS* is adjusted hand surface area for each subgroup (square meters), *SEF* is saliva extraction factor, and *bw* is body weight (kilograms). Total hand dermal exposure was determined using the PHED database and the assumptions discussed above. The hand surface area of toddlers (2–3 years of age) was assumed to be 0.035 $m^2$, which represents the 50th percentile total surface area values for males and females in the 2–3 and 3–4 year age groups, multiplied by the mean percentage of the total body represented by hands for males and females of that age (U.S. EPA 1996). The hand surface area for infants was assumed to be 0.007 $m^2$ and was also calculated as a percent of total body surface area for infants (U.S. EPA 1996). We calculated the total body surface area of infants using the formula by Current (1998). We assumed that, on the day of application, 50% of the insecticide deposited on the hand was available through saliva extraction (U.S. EPA 2005a, 2005c).

**Acute ingestion of garden produce.** We assumed that the insecticide settled onto a tomato garden and that the resident picked, processed, and ate tomatoes the next day. The estimated maximum insecticide residue deposited on tomatoes is discussed above. We assumed that the resident did not wash the tomatoes after picking. The residue concentration also did not change with processing of the tomatoes. The amount of insecticide ingested was estimated as the product of the residue concentration and the quantity of food consumed. Tomato consumption patterns were determined using the Dietary Exposure Evaluation Model [(DEEM)-Food Commodity Intake Database (FCID) version 2.04; Exponent, Washington, DC]. The model determines dietary consumption for the U.S. population and several subgroups by using individual food consumption records collected by the U.S. Department of Agriculture (USDA) Continuing Surveys for Food Intake by Individuals for 1994–1998. Translation factors used to convert foods-as-eaten to commodities are based on a U.S. EPA/USDA FCID recipe set. For this assessment, we determined the acute food consumption patterns by subgroup using the 95th percentile 1-day consumption values for tomatoes, tomato baby food, tomato paste, tomato paste baby food, tomato puree, tomato puree baby food, dried tomato, dried tomato baby food, and tomato juice. Therefore, the respective individuals in these subgroups ate all of these tomato food products within 1 day of application at the 95th percentile of U.S. national consumption.

***Subchronic exposure.*** We assumed multiroute exposures per day over 90 days after multispray events. Routes of insecticide exposure included inhalation, dermal contact with spray, ingestion of garden produce, hand-to-mouth ingestion by infants and toddlers from spray deposition on hands, hand-to-mouth ingestion by infants and toddlers from deposition on surfaces, dermal contact with soil and other surfaces, and soil ingestion.

**Subchronic inhalation, dermal, and hand-to-mouth exposures.** Exposures for each exposure type were estimated as

$$PE = (PE_{acute,\ type} \times SE) \div D, \quad [5]$$

where *PE* is the potential exposure (milligrams per kilogram bw per day), $PE_{acute,\ type}$ is the acute exposure type (e.g., acute inhalation) from each spray event (milligrams per kilogram bw), *SE* is the number of spray events, and *D* is the duration of exposure (days). We assumed that the insecticides were sprayed on days 1, 4, 14, 17, 27, 30, 40, 43, 53, and 56 (10 spray events per season) in any given area. The exposure duration was 90 days.

**Subchronic hand-to-mouth exposure from deposition on surfaces.** Subchronic hand-to-mouth exposures were estimated for only two subgroups (toddlers and infants) based on the rationale discussed above. Exposures were calculated as

$$PE = (EEC \times SEF \times SA \times DR \times FA \times D) \div bw, \quad [6]$$

where *PE* is potential exposure (milligrams per kilogram bw per day), *EEC* is the 90-day average environmental concentration of the active ingredient deposited on soil or turf within 91.4 m from the spray source (milligrams per square meter), *SEF* is saliva extraction factor, *SA* is surface area for three fingers (square meters), *DR* is dislodgeable residue, *FA* is frequency of activity (events per hour), *D* is exposure duration (hours), and *bw* is body weight (kilograms). Assumptions for estimating subchronic environmental concentrations are discussed above. The saliva extraction factor was assumed to be 50% (U.S. EPA 2005a, 2005c), and the palmar surface area for three fingers was assumed to be 20 $cm^2$ (U.S. EPA 2005c). Dislodgeable insecticide residue from soil or turf grass was assumed to be 20% (U.S. EPA 1997). The frequency of hand-to-mouth activity in children was assumed to be 20.5 events/hr and is based on the maximum frequency observed (Freeman et al. 2005). The duration of exposure was assumed to be 4 hr/day. Therefore, the toddler or infant was assumed to be engaging in hand-to-mouth activities outside each day for 4 hr over 90 days.

**Subchronic ingestion of garden produce.** Our assumptions for subchronic ingestion of garden produce were the same as for acute ingestion of produce, with the following differences: *a*) the insecticide was deposited onto both tomatoes and head- and leaf-lettuce, *b*) all tomato and lettuce consumption by the residents over the 90 days was from the garden, and *c*) tomato and lettuce consumption patterns were determined using chronic food consumption patterns (3-day average).

**Subchronic dermal contact with soil and other surfaces.** Exposures from contact with soil, turf, and other outdoor surfaces were calculated as

$$PE = (EEC \times SA \times SS \times AB \times DR \times CF) \div bw, \quad [7]$$

where *PE* is potential exposure (milligrams per kilogram bw per day), *EEC* is the 90-day average environmental concentration of the active ingredient deposited on soil or turf within 91.4 m from the spray source (milligrams per square meter), *SA* is body surface area in contact with surface (square centimeters), *SS* is weight of soil adhered to skin (milligrams per square centimeter), *AB* is dermal absorption rate, *DR* is dislodgeable residue, *CF* is the conversion factor to account for square meters to square centimeters, and *bw* is body weight (kilograms). The body surface area in contact with the surface was assumed to be the sum of surface areas for face (head ÷ 2), hands, arms, legs, and feet (U.S. EPA 1996). Therefore, we

assumed residents were minimally clothed while outside. Contact with surfaces was associated with certain human activities. The activities were assumed to be gardening for adults (0.55 mg soil/cm$^2$ skin) and soccer for children, including infants (0.164 mg soil/cm$^2$ skin) (U.S. EPA 1996). We assumed that these activities occurred each day over the 90 days. The assumptions for dermal absorption rate and dislodgeable residues are discussed above.

**Subchronic soil ingestion.** Exposures from incidental ingestion of soil were calculated as

$$PE = [(EEC \div SW) \times SI] \div bw, \qquad [8]$$

where *PE* is potential exposure (milligrams per kilogram bw per day), *EEC* is the 90-day average environmental concentration of the active ingredient deposited on soil or turf within 91.4 m from the spray source (milligrams per square meter), *SW* is soil weight (milligrams per cubic meter), *SI* is soil ingestion (milligrams per day), and *bw* is body weight (kilograms). Because the insecticide would only be surface-deposited on soil, we assumed that the concentration (milligrams per square meter) would be the same for a cubic meter of soil. Soil weight was assumed to be 3.86 kg/m$^3$ based on reported densities for Scotts lawn soil (The Scotts Company, Marysville, OH). Soil ingestion rates were assumed to be 100 mg/day for children and 50 mg/day for adults (U.S. EPA 1996). We assumed that all soil ingestion each day was from soil containing residues of the active ingredients.

***Risk characterization.*** Human-health risks in this study were assessed by integrating toxicity and exposure. We assessed risks using the risk quotient (RQ) method. For each population subgroup, an RQ was calculated by dividing the PE by the appropriate toxicity end point (e.g., the RfD). Therefore, the RQ is the ratio of exposure to effect. RQs < 1 are typically below regulatory levels of concern.

Exposures by similar route of exposure and duration (e.g., subchronic dermal contact with spray and surfaces) were compared with the appropriate RfD (e.g., subchronic dermal RfD). Multiroute exposures (dermal + ingestion + inhalation) were compared with the ingestion RfD. The ingestion RfD provided a conservative toxicity end point because it typically was based on the most sensitive NOAEL. Therefore, it represented the largest dose in which no adverse effects on human health would occur during the relevant exposure duration.

## Results

***West Nile virus risks.*** According to a seroepidemiologic survey conducted by Mostashari et al. (2001), for every diagnosed case of West Nile (WN) meningoencephalitis, there were approximately 30 additional people with WN fever, and approximately 2.6% of the population in outbreak areas in New York were infected during the epidemic of 1999. Loeb et al. (2005) reported a 3.1% outbreak infection rate in Oakville, Ontario, Canada, in 2002. Unfortunately, the seroprevalence of WNV antibodies across larger time and geographic scales has not been determined. Overall, 20% of infected persons develop mild febrile illness (Mostashari et al. 2001), and 0.67% develop neurologic disease (Fratkin et al. 2004). A total of 0.43% develop encephalitis, and 0.24% develop meningitis (Asnis et al. 2001; Brilla et al. 2004; Emig and Apple 2003; Klee et al. 2004; Sejvar et al. 2003a; Weiss et al. 2001).

Case-fatality rates in the United States ranged from 4 to 18% among hospitalized patients (Brilla et al. 2004; Emig and Apple 2003; Nash et al. 2001b; Pepperell et al. 2003; Sejvar et al 2003a; Weiss et al. 2001) and from 2.7 to 14% among cases reported to the CDC (CDC 2004b).

No difference in distribution of WNV infection among age groups and between sexes is apparent (Nash et al. 2001a, 2001b; Tyler 2001), but for unknown reasons, males seem to be at higher risk for WN neuroinvasive illness (O'Leary et al. 2004; Petersen and Marfin 2002). Children infected with WNV usually show no symptoms or have only a mild fever (Hayes and O'Leary 2004). The incidence of encephalitis and death increases with age (Nash et al. 2001a, 2001b; O'Leary et al. 2004; Tsai et al. 1998; Weinberger et al. 2001). Weiss et al. (2001) reported that persons ≥ 50 years of age were more likely to present meningoencephalitis and had increased mortality rates; other reports show that the incidence of neurologic symptoms and death may increase 10- to 20-fold among persons ≥ 50 years of age (Nash et al. 2001a; Sampathkumar 2003; Tyler 2001). The risk increases 43 times for persons ≥ 80 years of age (Sampathkumar 2003).

Few data exist regarding long-term morbidity after WNV infection. Substantial morbidity may follow hospitalization for WNV infection (Petersen et al. 2003) and is observed in patients with WN fever (Watson et al. 2004). Encephalitis cases seem to have more variable outcomes than meningitis cases, which tend to recover well (Granwehr et al. 2004). A poor prognosis and very limited recovery have been observed in acute flaccid paralysis cases (Saad et al. 2005; Sejvar et al. 2003a, 2003b).

Although patients with WN fever tend to recover well, median recovery time was 60 days for patients in Illinois in 2002 (Watson et al. 2004). The disease also has a significant effect on the lifestyle of patients with WN fever. Of 98 respondents with WN fever, 57 (58%) missed work/school, 82 (84%) had household activities limited, 47 (49%) had difficulty walking, and 89 (91%) had outside-of-home activities limited (Watson et al. 2004).

In a long-term follow-up study on 42 WN encephalitis survivors 1 year after illness onset, only 37% presented full physical, functional, and cognitive recoveries, and there was a substantially higher prevalence of impairment compared with baseline (Nash et al. 2001a). Similarly, only 2 of 8 patients in a study in New York presented full recovery after 1 year; 3 patients had neurologic sequelae, and 1 patient had minimal impairment after 18 months (Asnis et al. 2001).

***Acute risks from insecticides.*** Table 3 shows the calculated RQs for each active ingredient in terms of total acute PE. Exposures and risks also were determined for each exposure route. Potential acute inhalation exposures of the six human subgroups to the adulticides ranged from 0.00011 to 0.0075 mg/kg bw, and the environmental concentrations were lower than

**Table 3.** Acute RQs for the active ingredients for each subgroup.[a]

| Subgroup | Malathion | Naled | Permethrin | Resmethrin | Phenothrin | Pyrethrins | Piperonyl butoxide |
|---|---|---|---|---|---|---|---|
| Adult males | 0.0076 | 0.1496 | 0.0020 | 0.0052 | 0.0004 | 0.0081 | 0.0004 |
| Adult females | 0.0079 | 0.1576 | 0.0021 | 0.0055 | 0.0004 | 0.0085 | 0.0004 |
| Children (10–12 years) | 0.0105 | 0.2123 | 0.0029 | 0.0072 | 0.0006 | 0.0113 | 0.0006 |
| Children (5–6 years) | 0.0177 | 0.3631 | 0.0049 | 0.0123 | 0.0010 | 0.0190 | 0.0009 |
| Toddlers (2–3 years) | 0.0225 | 0.4726 | 0.0063 | 0.0159 | 0.0013 | 0.0245 | 0.0012 |
| Infants (0.5–1.5 years) | 0.0188 | 0.4495 | 0.0058 | 0.0147 | 0.0012 | 0.0218 | 0.0010 |

[a]RQ = total acute PE ÷ RfD.

**Table 4.** Subchronic RQs for the adulticides for each subgroup.[a]

| Subgroup | Malathion | Naled | Permethrin | Resmethrin | Phenothrin | Pyrethrins | Piperonyl butoxide |
|---|---|---|---|---|---|---|---|
| Adult males | 0.0360 | 0.0259 | 0.0007 | 0.0004 | 0.0001 | 0.0056 | 0.0032 |
| Adult females | 0.0363 | 0.0269 | 0.0007 | 0.0004 | 0.0001 | 0.0056 | 0.0032 |
| Children (10–12 years) | 0.0470 | 0.0290 | 0.0008 | 0.0005 | 0.0001 | 0.0074 | 0.0043 |
| Children (5–6 years) | 0.0676 | 0.0447 | 0.0012 | 0.0009 | 0.0002 | 0.0104 | 0.0059 |
| Toddlers (2–3 years) | 0.1815 | 0.1294 | 0.0204 | 0.0037 | 0.0009 | 0.0270 | 0.0262 |
| Infants (0.5–1.5 years) | 0.2074 | 0.1661 | 0.0301 | 0.0054 | 0.0013 | 0.0292 | 0.0325 |

[a]RQ = total subchronic PE ÷ RfD.

the inhalation reference concentrations for all active ingredients evaluated. Potential acute dermal exposures to the adulticides ranged from 0.0000001 to 0.0011 mg/kg bw, with RQs ranging from 0.0000005 to 0.0113. For acute exposure due to ingestion (hand-to-mouth exposure from spray deposition on hands and ingestion of produce), total PEs ranged from 0.0001 to 0.0061 mg/kg bw, with RQs ranging from 0.00014 to 0.2142. Total acute RQs ranged from 0.0004 to 0.4726.

***Subchronic risks from insecticides.*** Table 4 shows the calculated RQs for each active ingredient in terms of total subchronic PE. Potential subchronic inhalation exposures of the six subgroups to the adulticides ranged from 0.000012 to 0.00083 mg/kg bw. For subchronic dermal exposures to the adulticides (dermal and contact with soil), total PEs ranged from 0.00000006 to 0.00015 mg/kg, with RQs ranging from 0.0000001 to 0.0015. Potential subchronic exposures due to ingestion (ingestion of produce and soil, hand-to-mouth activity after contact with surfaces, and hand-to-mouth activity after contact with spray drift) ranged from 0.00001 to 0.0283 mg/kg bw, with RQs ranging from 0.00007 to 0.1709. Total subchronic RQs ranged from 0.00014 to 0.2074.

None of the subgroups had RQs ≥ 1.0 (i.e., PEs did not equal or exceed the RfDs) for any of the active ingredients evaluated. The lowest acute RQs were to phenothrin and piperonyl butoxide for adults and the highest acute RQ was to naled for toddlers (Table 3). The lowest and highest subchronic RQs were to phenothrin for adults and malathion for infants, respectively (Table 4).

## Discussion

***Conservatism.*** Based on the exposure and toxicity assumptions above, we believe our assumptions were sufficiently conservative and most likely overestimated risk. For example, assuming an acute RR of 0.8 $m^3$/hr for 2 hr and no dermal or ingestion exposures [which were the U.S. EPA assumptions for mosquito control uses of permethrin (U.S. EPA 2005c)], there would be a 90% reduction in exposure for toddlers compared with our value. Indeed, draft tier 1 risk assessments recently conducted for malathion, piperonyl butoxide, pyrethrins, and permethrin by the U.S. EPA also suggest that our results are sufficiently conservative (U.S. EPA 2000c, 2005a, 2005b, 2005c). Because of the conservative exposure assumptions used, we believe higher-tiered risk assessments using more realistic exposures would result in risk values significantly lower than those presented here.

The conservatism of our risk assessments for insecticides used in adult mosquito control is supported by residential biomonitoring and epidemiologic studies. Currier et al. (2005) assessed human exposure to ULV-applied naled, permethrin, and phenothrin in Mississippi, North Carolina, and Virginia as a result of emergency large-scale mosquito abatement. Using biomonitoring of urine, they did not observe an increase in insecticide metabolite concentrations among exposed residents. Karpati et al. (2004) and O'Sullivan et al. (2005) did not observe increases in hospital emergency department visits for asthma after wide-scale spraying of residential neighborhoods.

***Uncertainties.*** Despite the conservatism of our risk assessment, uncertainties were revealed. Many of the uncertainties associated with residential exposure estimates are discussed above. The principal uncertainty was for environmental concentrations of the active ingredients. Data for actual aerial concentrations and surface deposition of active ingredients need to be generated to more accurately characterize risks. Because of the nature of ULV application methods, it is likely that concentrations of active ingredients are much lower than those predicted using the AERMOD and ISCST3 tier 1 models. Toxicologic uncertainties include mammalian toxicities to combinations of piperonyl butoxide and adulticides and to inert ingredients in the formulated products. The addition of piperonyl butoxide to the adulticides increases the mosquito toxicity of the pyrethroids approximately 10-fold, but mammalian toxicity is not likely to be proportionally increased (Knowles 1991). Even if mammalian toxicity were increased 10-fold to the pyrethroids, RQs would still be well below levels of concern. Human exposures to solvents and other inert ingredients are likely to be low, resulting in low risks (NYCDOH 2001). Future research should be directed toward reducing toxicity and exposure uncertainties associated with mosquito adulticides. In addition, future assessments should address ecologic risks.

***Comparing risks.*** Although it is difficult to compare the risks directly, several conclusions can be drawn by considering both human risks from exposure to WNV and insecticides used to control adult mosquitoes. In a situation where application of mosquito adulticides occurs because of known human cases of WNV, an adult human female may have at least a 3% probability of being infected by WNV. An adult female in that same area conservatively may have a 100% probability of being exposed to a particular mosquito adulticide. Her probability of exposure to the insecticide may be greater than WNV infection, but the consequences (i.e., the risks) of the exposures would be very different. Once infected with WNV, an adult human female has approximately a 20% probability of expressing clinical signs of illness (WN fever) and, depending on age, a 0.67% probability of expressing neurologic disease. Depending on the insecticide, her acute exposure would be 0.0415–15.76% of the RfD (0.0004–0.1576% of the NOAEL). Consequently, her acute risks from the insecticide would be lower than her acute risks from WNV. Subchronic insecticide risks would also be negligible (Table 4), whereas subchronic and chronic WNV risks (disease sequelae) would be greater. Therefore, once exposed to the insecticide (based on the tier 1 exposure assumptions from this study), the risk of any adverse health effects to the adult female would be negligible.

Results from our risk assessment and the current weight of scientific evidence (Currier et al. 2005; Karpati et al. 2004; NYCDOH 2001; O'Sullivan et al. 2005; U.S. EPA 2000c, 2005a, 2005b, 2005c) indicate that human-health risks from residential exposure to mosquito adulticides are very low and are not likely to exceed levels of concern. Further, by virtually any current human-health measure, the risks from infection by WNV exceed the risks from exposure to mosquito insecticides. Therefore, perceptions that human-health risks from the insecticides used to control adult mosquitoes are greater than the risks from WNV currently cannot be supported by current scientific evidence. Our results, and the results from other studies, should be used by the U.S. EPA, public health officials, and the general public to make better-informed decisions about risk–risk tradeoffs.

### Correction

In the original manuscript published online, the acute air concentration for naled in Table 2 and the RQ ranges for acute inhalation exposures and acute subchronic dermal exposures were incorrect. These have been corrected here.

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