EVALUATION OF MALARIA SURVEILLANCE USING RETROSPECTIVE, LABORATORY-BASED ACTIVE CASE DETECTION IN FOUR SOUTHWESTERN STATES, 1995

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Abstract. The global resurgence of malaria has raised concerns of the possible reintroduction of indigenous transmission in the United States. The Centers for Disease Control and Prevention’s National Malaria Surveillance System, using data supplied by state and local health departments (SLHDs), is maintained to detect local malaria transmission and monitor trends in imported cases. To determine the completeness of reporting of malaria cases to SLHDs, cases identified by local surveillance systems were compared with those identified through active case detection conducted at all laboratories that receive clinical specimens from 11 metropolitan areas in Arizona, California, New Mexico, and Texas. Of the 61 malaria cases identified through either local surveillance or active case detection, 43 (70%) were identified by SLHDs (range by metropolitan area = 50–100%) and 56 (92%) through active case detection. High percentages of cases were identified by SLHDs in New Mexico (80%) and San Diego County (88%), where laboratories are required to send positive blood smears to the SLHD laboratory for confirmation. Completeness of reporting, calculated using the Lincoln-Peterson Capture-Recapture technique, was 69% for SLHD surveillance systems and 89% for laboratory-based active case detection. The high percentage of cases identified by the 11 SLHDs suggests that the National Malaria Surveillance System provides trends that accurately reflect the epidemiology of malaria in the United States. Case identification may be improved by promoting confirmatory testing in SLHD laboratories and incorporating laboratory-based reporting into local surveillance systems.

Reports by the Institute of Medicine and the Centers for Disease Control and Prevention (CDC) on emerging infectious diseases have highlighted the potential for reintroduction of mosquito-borne malaria transmission in the United States, which had been interrupted during the 1940s.1,2 Fueling these concerns are published reports of more than 60 outbreaks of locally acquired mosquito-borne malaria in the United States since the mid-1950s.3–7 During the last decade, the frequency of these outbreaks has increased and outbreaks are now occurring in urban and suburban areas and northern locations, such as New York City, Houston, and Michigan.4–6 In their strategy for responding to new and re-emerging infectious disease threats, CDC has given priority to enhancing surveillance systems to improve public health officials’ ability to detect and respond rapidly to outbreaks and identify changes in the pattern of diseases of major public health importance.2 The National Malaria Surveillance System (NMSS) is maintained by CDC to detect cases of malaria acquired in the United States, monitor trends in malaria acquired in other countries (imported malaria), and guide CDC recommendations on chemoprophylaxis for international travelers. Currently, all 50 states, New York City, and the District of Columbia voluntarily provide reports of malaria cases to CDC.

The ability of a surveillance system to detect outbreaks and monitor epidemiologic trends depends on its sensitivity (i.e., the percentage of all diagnosed cases of a disease that are identified by the surveillance system).8 Because persons with malaria in the United States may occasionally be misdiagnosed, be treated without blood-slide confirmation, or treat themselves without seeking medical attention, there is currently no gold standard by which the sensitivity of malaria surveillance can be assessed. An evaluation in 1994 comparing malaria cases reported to three state health departments to cases identified through hospital discharge databases found that state health departments had identified 28% of cases in the discharge database in New York, 53% in New Jersey, and 81% in California (Centers for Disease Control and Prevention, unpublished data). Laboratory-based active case detection has been used to define the extent of an outbreak of locally acquired malaria in New York City in 1993, Houston, Texas in 1994, and Michigan in 1995.4,5,7 Thirteen (93%) of 14 cases diagnosed at least one week before the start of the investigation in New York City had been reported to the health department. In contrast, only 19% of 21 cases identified through active case detection had been reported to the Houston Department of Health and Human Services. Similarly, the Michigan surveillance system had only received reports of 20% of cases identified through the laboratory survey. Of additional concern, the Houston investigation identified two patients with malaria who reported travel solely to cities in the United States–Mexico border region, an area that is not considered to have endemic transmission.

The low percentage of malaria cases identified in Houston and Michigan has raised questions about the overall sensitivity of NMSS. This investigation was conducted to determine the sensitivity of malaria surveillance in several large metropolitan areas. Sites were chosen in the four states bordering Mexico to investigate whether there was additional evidence of the possible reintroduction of endemic transmission in the United States–Mexico border area (e.g., cases of malaria in persons who had only traveled within the border region).

MATERIALS AND METHODS

Eleven metropolitan areas were nonrandomly selected for study based on their location in the border area, population
size, and the annual number of malaria cases reported. No health department declined participation in this assessment. Sites included were Tucson and metropolitan Phoenix, Arizona; San Diego and Imperial Counties, California; Albuquerque, Las Cruces, Santa Fe, and Española, New Mexico; and Houston/Harris County, Cameron County (including Brownsville), and El Paso, Texas. Lists of hospital and commercial laboratories accepting clinical specimens from these 11 metropolitan areas, including those located outside the study sites, were obtained from state and local health department (SLHD) staff and supplemented by a search of the local yellow pages and informal interviews with laboratory personnel contacted during the investigation. Laboratories were contacted by telephone or visited to determine whether they performed blood smear examinations for malaria. Some specialized laboratories (e.g., drug testing laboratories) were not contacted. If smear examinations were performed, laboratories were requested to search their records and provide identifying information on all patients who had malaria diagnosed by blood smear from January 1 through August 21, 1995.

Records of each SLHD were then reviewed to determine whether cases identified by active case detection had also been identified by the health department. For cases not previously identified, information to complete NMSS case report forms was obtained by either SLHD staff or CDC investigators through medical record reviews or interviews with the treating physicians. Data collected on each patient included the date of diagnosis, species identification, country and dates of travel, and type of malaria chemoprophylaxis taken.

Annual cumulative incidence was estimated by using a linear extrapolation from the total number of cases identified in the eight-month study period to determine the estimated number of malaria cases per year for each study site. This estimate was divided by population estimates obtained from the 1994 U.S. Bureau of Census data yielding a measurement of cumulative incidence per 100,000 population per year. Annual cumulative incidences were calculated for each state, except for Texas where Houston/Harris County was analyzed separately due to the large number of cases identified at that site. Patient information was entered into a computer database and summary statistics calculated using Epi Info 6.02.

To determine completeness of coverage of the SLHD surveillance system and laboratory-based active case detection, the Lincoln-Peterson capture-recapture method was used to calculate the probable number of cases of malaria in the population. The Lincoln-Pearson capture-recapture formula is \( N = \frac{[R + 1] \times (S + 1)}{(C + 1)} - 1 \), where \( N \) = the number of cases in the population, \( R \) = the number of cases identified by SLHD, \( S \) = the number of cases identified by laboratory-based active case detection, and \( C \) = the number of cases identified by both methods. This technique compares the number of cases of a single disease identified by two or more distinct surveillance systems to generate an estimate of the total number of cases of a disease in a population. Completeness of coverage, the percentage of total estimated cases identified by a surveillance system, was then calculated by dividing the number of cases identified by each method by the calculated number of probable cases in the population.

**RESULTS**

Of the 282 laboratories contacted for information that serve these 11 metropolitan areas, 154 (55%) reported that they performed blood smear examinations for malaria. Fourteen of these laboratories were located geographically outside these 11 metropolitan areas, including six that were outside the four state region. Thirty-four (22%) of 154 laboratories had identified at least one positive blood smear during the study period. Two laboratories reported that they performed blood smear examinations for malaria, but did not supply case information to the investigators.

A total of 61 patients with blood smear-confirmed malaria were identified in the 11 locations during the eight-month study period. Eighteen (30%) cases were identified only by laboratory-based active case detection, five (9%) were identified only by the SLHD, and 38 (62%) were identified by both. Overall, laboratory-based active case detection identified 56 (92%) patients with malaria, while SLHDs identified only 43 (70%) cases. With the exception of one case diagnosed in early August 1995, all cases not identified by SLHDs were diagnosed from one to seven months before this evaluation, allowing adequate time for reports to have been received by SLHDs. Of the five cases that were not identified by active case detection, four were diagnosed at laboratories that had participated in the active case detection survey and three of the four had identified other cases of malaria to the investigators. The fifth patient was diagnosed by an emergency room physician, who had prepared and examined the blood smears himself, but did not send the slides to a laboratory for confirmation.

Of the 61 patients with malaria, more than half (N = 35) were diagnosed in Houston/Harris County (Table 1). Estimated annual cumulative incidence ranged from 0.43 per 100,000 population per year in San Diego and Imperial

### Table 1

<table>
<thead>
<tr>
<th>Location</th>
<th>Total number of cases</th>
<th>Cases per 100,000 population per year</th>
<th>Cases identified by SLHDs No. (%)</th>
<th>Cases identified by laboratory survey No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arizona (Metro Phoenix and Tucson)</td>
<td>10</td>
<td>0.52</td>
<td>5 (50%)</td>
<td>9 (90%)</td>
</tr>
<tr>
<td>California (San Diego and Imperial Counties)</td>
<td>8</td>
<td>0.43</td>
<td>7 (88%)</td>
<td>7 (88%)</td>
</tr>
<tr>
<td>New Mexico (Espanola, Albuquerque, Santa Fe, and Las Cruces)</td>
<td>5</td>
<td>1.29</td>
<td>4 (80%)</td>
<td>5 (100%)</td>
</tr>
<tr>
<td>Houston/Harris County, Texas</td>
<td>35</td>
<td>1.77</td>
<td>24 (69%)</td>
<td>32 (91%)</td>
</tr>
<tr>
<td>El Paso and Cameron County, Texas</td>
<td>3</td>
<td>0.50</td>
<td>3 (100%)</td>
<td>3 (100%)</td>
</tr>
<tr>
<td>Total</td>
<td>61</td>
<td>1.22</td>
<td>43 (70%)</td>
<td>56 (92%)</td>
</tr>
</tbody>
</table>

* Calculations were based on an estimate of the annual number of cases and used population data obtained from U.S. Bureau of the Census.4
Cases were identified (mean 50±60%). There was a trend toward a higher percentage of reported cases in SLHDs where identiﬁed 88–100% of the cases. There was a trend toward one of three countries: 14 (23%) to Nigeria, 10 (16%) to Honduras, and eight (13%) to India (Table 2). One congenital infection was diagnosed in a 26-day-old infant born to a recent immigrant from Nigeria. Travel histories could not be obtained on two individuals. Of the three (5%) individuals who reported traveling only in Sonora State, which borders the United States. Detailed travel history on the third individual was unavailable.

Only 12 (20%) persons had reported taking chemoprophylaxis during travel; six had not taken medications recommended by CDC for their area of travel and information was not available for one other. Of the five persons who took CDC-recommended medications for chemoprophylaxis, four reported non-adherence with their regimens and one had a relapse infection of *P. vivax*.

The Lincoln-Peterson capture-recapture method was used to estimate the number of patients with malaria that could have been missed by both the existing surveillance systems and laboratory-based active case detection. Using this method, it was estimated that the total number of diagnosed cases of malaria in all 11 metropolitan areas during the eight-month assessment period was 62 (95% conﬁdence interval = 60.3–64.0). Using this point estimate, only one blood smear-positive case would have been missed during this evaluation. The adjusted percentages of cases identiﬁed (completeness of coverage), based on this estimate of 62 total cases, were 69% for SLHD surveillance systems and 89% for laboratory-based active case detection.

**DISCUSSION**

A primary goal of a surveillance system is to collect representative data on the occurrence of a disease in a population that enables public health ofﬁcials to make decisions on what interventions are needed to meet their objectives for prevention and control. After malaria transmission was interrupted in the United States, NMSS was established to identify episodes of domestic transmission and monitor trends in imported disease. Because malaria is rarely acquired in the United States (< 10 cases per year), NMSS should be highly sensitive to detect such rare occurrences. Evidence that NMSS has met these goals include its detection of more than 60 episodes of probable mosquito-borne transmission since the late 1950s, the recognition of the first case of chloroquine-resistant *P. falciparum* in Africa, and identiﬁcation of a decrease in *P. falciparum* cases acquired in Africa after a change in CDC’s recommendations for chemoprophylaxis for travelers to that area.

Our study provides further evidence that suggests that NMSS provides accurate trends in the epidemiology of malaria in the United States. In the 11 locations studied, SLHDs had identiﬁed 70% of all malaria cases detected during this evaluation. This percentage compares favorably with reported percentages of cases identiﬁed by surveillance systems for diseases with similar objectives for control. Although there may be wide variability in completeness of reporting among SLHDs in other regions and one must be cautious in extrapolating these data, the results of this study provide further evidence that NMSS is sensitive for detecting cases of malaria diagnosed in the United States.

Although the percentage of cases identiﬁed was high, we identiﬁed some deﬁciencies in malaria case reporting and approaches that could be more widely applied to improve the case identiﬁcation by local surveillance systems and
NMSS. Differences were noted in the percentage of cases identified from one study site to another, possibly due to the differing structures of the local surveillance systems. Sensitivities were high in New Mexico and San Diego, where clinical laboratories are required to send all positive blood smears to the health department laboratories for confirmatory testing. The health departments in most other study locations relied almost entirely on self-initiated case reports from infection control practitioners and physicians. Promotion of voluntary confirmatory testing by SLHD laboratories should be considered by other health departments as a mechanism to improve case identification. More widespread use of state, local, and CDC reference laboratories could also reduce the number of cases where the infecting species could not be determined.

More cases were identified by laboratory-based active case detection than by SLHD surveillance systems, with the exception of San Diego County, which already uses laboratory-based reporting. These findings add additional support to initiatives currently under way in a number of states to incorporate laboratory-based reporting into their existing surveillance structures. Recent improvements in communications through facsimile and electronic mail may facilitate the implementation of these systems with a minimal investment of resources. The implementation of laboratory-based reporting may also lead to a reduction in the time delay from diagnosis to when the case is identified by the health department. During the course of this assessment, many local health department personnel indicated that, in their experience, the delay between diagnosis and identification by the health department was usually several weeks.

This assessment also documented an increase in the percentage of cases identified by the Houston Department of Health and Human Services from 19% in 1994 to 69% in 1995. This improvement most likely resulted from a heightened awareness of malaria reporting, which was stimulated by publicity and intensified educational programs by the health department after an outbreak of locally acquired malaria in 1994. The increase in percentage of cases identified after this effort suggests that even short-term efforts to raise public awareness of the importance of reportable disease surveillance can result in long-lasting improvements in case detection.

It was noted during this study that many commercial clinical laboratories are merging into large national chains and centralizing their specialized testing, including malaria blood slide examinations. Six laboratories we surveyed were located in other states, including one located in New Jersey. As this trend toward consolidation of laboratory services continues, SLHDs will need to ensure that out-of-state laboratories are reporting back smear-confirmed cases. Close monitoring will also be needed to make certain that diagnosis and treatment are not delayed by sending specimens these long distances.

One limitation of this study was the inability to determine with certainty the actual number of malaria cases diagnosed during the study period in the locations we evaluated. Although our calculations using the Lincoln-Peterson capture-recapture technique indicate that a very small number of cases were probably missed, these estimates are based on the assumption of static populations in the study locations.

In particular, the sensitivity of NMSS for detecting cases of malaria in mobile populations, such as migrant farm laborers and undocumented aliens, may be much lower and warrants further investigation. Laboratory-based active case detection also would not have identified cases of malaria that were diagnosed by clinical criteria, without blood smear confirmation, or cases in which individuals self-treated without seeking medical attention. It remains unclear how common these practices are in the United States. In addition, we cannot rule out the possibility that the higher percentage of cases identified in New Mexico and San Diego resulted because the methodology used for this assessment and the surveillance systems in these locations were both based on cases identified by laboratories, potentially yielding data that are not independent. The Lincoln-Peterson capture-recapture technique assumes that the data being compared are collected by independent methods.

At least one person with malaria that we identified during this evaluation had traveled only to Sonora State in Mexico, which is not considered a malaria risk area. This supports concerns of possible reintroduction of mosquito-borne malaria transmission in the United States-Mexico border area that were raised after the outbreak investigation in Houston, where two malaria cases were identified in individuals who reported having only traveled in this region. In light of the re-emergence of other mosquito-borne diseases in northern Mexico, such as dengue, further investigation into the risk of reintroduction of malaria transmission in this region is warranted.

Acknowledgments: We thank the following persons for assistance with data collection and coordination: Dr. Rose Lee Bell and Janeen Cousins (Houston Department of Health and Human Services, Houston, TX); Dr. Katherine A. Hendricks (Texas Department of Health, Austin, TX); Lawrence Sands (Arizona Department of Health Services, Phoenix, AZ and Maricopa County Department of Health Services, Phoenix, AZ); Dr. Duc Vugia and Dr. Steve Waterman (California Department of Health Services, Berkeley, CA); Dr. Mack Sewell and Martha Tanuz (New Mexico Department of Health, Santa Fe, NM) Dr. Gustavo Stern (Cameron County Board of Health, Brownsville, TX); and Jorge Gallegos (El Paso City-County Health Department, El Paso, TX).

Financial support: Funding for this study was provided by the CDC National Centers for Infectious Diseases Emerging Infections Program.


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REFERENCES


