ACUTE COMMUNICABLE DISEASE CONTROL

SPECIAL STUDIES REPORT
2000

County of Los Angeles
Department of Health Services

Public Health Programs
Disease Control Programs

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Acute Communicable Disease Control Unit
313 N. Figueroa Street, Room 212
Los Angeles, CA 90012
(213) 240-7941

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CONTRIBUTORS

Acute Communicable Disease Control . . . . . Laurene Mascola, MD, MPH

Immunization Program . . . . . Cheri Todoroff, MPH

Pediatric Spectrum of HIV Disease Study . . . . . Toni Frederick, PhD

Varicella Active Surveillance Project . . . . . Carol Peterson, MD, MPH

Enhance Surveillance Project . . . . . David Dassey, MD, MPH

Acute Communicable Disease Special Reports

Editor . . . . . Rachael Lee, RN, BSN

Style Editor . . . . . Esther Parker

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A CASE OF BAYLISASCARIS PROCYONIS (RACCOON ROUNDWORM) MENINGOENCEPHALITIS, LOS ANGELES, 2000

In January 2000, a 17 year old male with severe developmental delay and a history of pica was admitted to a local hospital in a coma. Two days prior to admission, he had become progressively drowsy with a decreased appetite. Upon admission he was diagnosed with eosinophilic meningoencephalitis and was treated with broad spectrum antibiotics, antiparasitic and antiviral drugs with no improvement. Two MRI scans revealed multiple abnormalities. A brain biopsy was consistent with *Baylisascaris procyonis* infection. Serum and spinal fluid were positive for *Baylisascaris procyonis* by IFA. The case-patient lived in a group home in the southern, urban part of Los Angeles County. Prior to his hospitalization, attendants at the group home noticed a raccoon in the neighborhood.

Acute Communicable Disease Control, with Veterinary Public Health, the Public Health Laboratory, and consultants from San Jose State University, initiated a public health investigation of this case to determine the source of the BP infection and to develop appropriate public health recommendations.

METHODS

We consulted with Animal Control about complaints of raccoons in the neighborhood where the patient lived. We made a thorough inspection of the four sites where the patient spent time in the 6 weeks before becoming ill. These included his permanent group home; a second, temporary group home; his mother's home; and the school that he attended Monday through Friday. We looked for evidence of raccoon activity including paw prints, scratches on trees, and raccoon latrines (sites raccoons use repeatedly to defecate). We collected raccoon feces, sand, and soil from where the case-patient was known to play for microscopic analysis.

RESULTS

The permanent group home was located on the edge of a residential neighborhood adjacent to an industrial and commercial area. Animal Control did not record any complaints of raccoons in the neighborhood during the 6 months prior to the patient's illness. Of the 4 places investigated, only patient's group home backyard and the adjoining backyard had evidence of raccoon activity including feces and raccoon tracks. Old raccoon feces were found in 2 sandboxes in the group home backyard and on the cement fence which enclosed the backyard. Multiple fresh raccoon latrines and fresh racoon tracks were found in the backyard adjacent to the group home.

Two sand and fecal samples were collected from the sandboxes, a soil sample was collected from the ground around the swingset, and 12 fecal samples were collected from the adjacent backyard and the top of the cement fence. All soil, sand and fecal samples from the yard where the case-patient played were negative. Infective-stage eggs were found by microscopic examination in 3

fecal samples from the adjacent backyard.

DISCUSSION

This is the first report of BP neural larva migrans in a semi-urban area and in an area previously unknown to local health authorities to have a raccoon problem. BP neural larva migrans is rare but should be considered whenever the diagnosis of eosinophilic meningoencephalitis is made, especially in young children or in those with developmental delay. Raccoon contact should be asked about. Clinicians may call the health department for help in obtaining the appropriate tests for BP. There have been no reports of successfully treating someone who is already symptomatic with neural BP; however, based on animal data, it may be possible to prevent such infections with antihelminthic treatment given a few days after exposure to infected raccoon feces.

Baylisascaris procyonis (BP) is a common roundworm of raccoons. It lives in the intestines of raccoon and lays millions of eggs daily that are passed in the raccoon feces. After approximately 2 to 4 weeks in the outside environment the eggs embryonate into infective larva. If humans ingest racoon feces after this time they may develop visceral, ocular or neural larva migrans. All of these are syndromes in which larvae travel throughout the body, eyes, or central nervous system respectively. Neural larva migrans is especially noteworthy due to its eosinophilic meningoencephalitis and peripheral eosinophilia. Thus far, there have only been 7 confirmed and 2 presumptive cases of BP neural larva migrans reported in the English medical literature. Five of the confirmed and one presumptive case were in children less than 18 months. One case occurred in a 21-year-old with developmental delay and pica, much like this case. The medical outcomes have been uniform: developmental delay among the infants, neurolgic disability, or death. All case-patients resided in rural or suburban neighborhoods.

Since the consequences of infection are so severe and pharmaceutical prevention is untested, the primary public health responsibility must be in preventing exposure to raccoon feces. As the population of Los Angeles County grows and as people build homes in new areas, contact with wild animals is inevitable. Raccoons are ubiquitous and cannot be eliminated so people must minimize their exposure to raccoons and raccoon feces. Raccoons should not be kept as pets. Food for animals should not be left outside and garbage containers should be tightly closed with latches that will prevent raccoons from taking off the lids. Children and anyone with developmental disabilities should be kept away from raccoons and areas where raccoons are prevalent. Sandboxes should be kept covered when not in use. Sixty to 80% of raccoons are infected with BP so raccoon feces must be assumed infective. Raccoon feces, which can be identified by the presence of undigested grain or paper or shiny, man-made objects, and raccoon latrines, often found in the forks of trees, or on raised surfaces such as woodpiles, a collection of rocks, or on walls or fences, should be collected and either burned or taken to a landfill. Care must be taken not to contaminate oneself; gloves should be used and clothes promptly washed. Fresh raccoon feces, distinguished by its shiny appearance, is not infective and should be disposed of immediately before the BP eggs become infective larva (in 2-4 weeks). Other contaminated surfaces may be treated with boiling

water.

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AN OUTBREAK OF *SALMONELLA* SEROTYPE THOMPSON ASSOCIATED WITH HAMBURGER BUNS

BACKGROUND

The Los Angeles County Department of Health Services (LAC DHS) received a report of a cluster of gastrointestinal illnesses associated with a catered luncheon serving two neighboring office buildings located in Whittier, CA. The luncheon was held July 14, 2000 at noon, and catered by a company located in Orange County. Hamburgers, chicken burgers, condiments, lettuce, tomatoes, fruit salad, cookies, lemonade and iced tea were served from two identically set buffet tables in the courtyard at one of the office buildings. LAC DHS Acute Communicable Disease Control Unit (ACDC) conducted an epidemiologic investigation of the outbreak. One ill person was confirmed as having *Salmonella* early in the investigation..

METHODS

Case Definition

An outbreak-associated salmonellosis case was defined as a person associated with the catered office building complex luncheon with (1) culture positive for *Salmonella* Ser. Thompson (ST) or (2) diarrhea and fever or (3) diarrhea and two or more of the following symptoms: nausea, vomiting, abdominal cramps, headache, body aches.

ACDC obtained a list of food items served at the luncheon. A standardized questionnaire was developed and distributed to all attendees. Supplemental questionnaires also were distributed for Sensitive Occupation/Situation (SOS) and additional exposure information. Following the discovery of a positive Salmonella group C1 case, stool specimens were requested from those attendees who reported illness and were working in an SOS. Two site visits were made. Data was analyzed using EpiInfo and SAS. Pulsed-field gel electrophoresis (PFGE) analysis was completed on available specimens of the culture-confirmed cases by LAC DHS Public Health Laboratory. Orange County Environmental Health inspected the catering company, while LAC DHS interviewed for additional information.

RESULTS

The number of persons attending the event was estimated to be 250. We were able to contact 202 individuals (81% response rate) for detailed information. A total of 47 individuals met a case definition: 35 clinical based on presentation of symptoms and 12 with laboratory confirmation. The most frequent symptoms reported by cases were diarrhea and cramps. Sixty-three percent reported fever. A detailed analysis of the case *Salmonella* Ser. Thompson isolates revealed indistinguishable patterns by PFGE technology.

Food-specific analysis indicated several food categories as suspect vehicles for infection, including

lemonade, hamburgers, hamburgers/chicken burgers and one of the buffet tables (Table A). A risk-ratio for the combined hamburger/chicken burger category could not be calculated, but all ill individuals reported eating either a hamburger or a chicken burger (Fisher-exact two-tailed p-value=0.3). Only Table A and lemonade were significantly associated ($p<0.05$) with illness in the crude risk ratio calculations. Stratified analysis of hamburger, lemonade, and cookie by Table A was performed in EpiInfo. Again, the statistics for the category including those exposed to either hamburger or chicken burger could not be calculated. Only hamburger had a risk ratio greater than one (RR=1.95, CI=1.06-3.59) among those exposed to Table A. However, 29% of the cases reported exposure to Table B. The logistic regression model included hamburger, lemonade, and Table A. Only Table A was significant in the regression model, with a risk ratio of 1.79 (CI=1.02-2.68).

Orange County Environmental Health Division inspected the catering company July 26, 2000 in Santa Ana, CA. The inspection report did not indicate any major violation which would contribute to the illness reported. The details of the food preparation and table set-up were obtained from an interview with the catering company's president.

The Multi-county Outbreak - a Missing Link

In August 2000, the California Department of Health Services identified an increase in case reports of ST involving Southern California counties. This illness cluster started during the same month as the office building complex, but involved sporadic cases of ST. The Southern California cases gave histories of eating a hamburger on a bun in a restaurant. Many of the cases, including 11 additional LAC cases, ate at different locations of a specific chain restaurant (Chain A) in Southern California and Arizona, as well as other restaurants in Southern California. The source of this outbreak was eventually determined by Orange County DHS to be a food worker who worked at Bakery B in Orange County. The bakery supplied hamburger buns to the caterer involved with the office building outbreak as well as to Chain A restaurants and other restaurants. A food worker at Bakery B was stool culture positive for ST, with an onset of illness July 13, 2000 and was reported to have worked while symptomatic. The job duties of this food worker included taking freshly baked buns off the rack, feeding them through a slicer, and then packaging the buns. This activity was done without the use of gloves. PFGE analysis of both the office building complex and the multi-county/state outbreak ST isolates and the food worker had indistinguishable patterns.

CONCLUSIONS

Salmonella Ser. Thompson was the etiologic agent responsible for the office building complex outbreak as well as the multi-county/state outbreak. The culture-positive Bakery B worker who handled the buns was the source of contamination of the buns which were supplied to the caterer and Chain A restaurants. The distribution of the buns to various commercial facilities extended the outbreak over a wide geographic area.

BUILDING A SURVEILLANCE SYSTEM FOR BIOTERRORISM AND COMMUNITY OUTBREAKS

The Use of Multiple Algorithms to Detect Unusual Increases in Hospital Admissions, Visits, and Deaths in Los Angeles County

BACKGROUND

Los Angeles city was scheduled to host the Democratic National Convention (DNC) in August 2000. By June 2000, Acute Communicable Disease Control Unit (ACDC) of the Los Angeles County Department of Health Services (LAC DHS) began collaborations with the Centers for Disease Control and Prevention (CDC) and the California State Health Department. By the time the Convention started, a team of approximately ten health professionals was conducting surveillance for certain symptoms suggestive of bioterrorism. Aiming for timeliness, the multi-agency team devoted many resources in terms of time and people.

An ACDC epidemiologist and graduate-level student worker proposed an alternate surveillance system. For simplicity of data collection and analysis, they decided to use daily counts of admissions, visits, and deaths, instead of counts of diagnostic codes for syndromic surveillance. Using established outbreak detection algorithms, the surveillance system would detect statistically significant (p 0.05) increases in the daily counts.

ACDC has conducted previous research on outbreak detection algorithms. Using four outbreak detection algorithms in studying campylobacteriosis, ACDC attempted to validate the algorithms retrospectively (Special Reports 1999). However, a prospective approach may be more appropriate for validation because outbreaks can be separated more easily between those detected by an increase in reports and those detected by a single phone call from a physician or patient describing a possible outbreak situation.

Thus, there were two proposed purposes for establishing this bioterrorism surveillance system. The first purpose was to explore using outbreak detection algorithms modified to analyze daily data instead of weekly data to alert when possible bioterrorist events or community outbreaks occur. The second purpose was to attempt to validate the algorithms prospectively.

METHODS

Data Collection

On July 1, 2000, under the directive of the former Associate Director of Clinical and Medical Affairs Harbor-UCLA Medical Center (Harbor), Martin Luther King/Drew Medical Center (KDMC), Los Angeles County+University of Southern California Medical Center (LAC+USC), and Olive View Medical Center (OVMC) started providing ACDC with daily counts of hospital admissions, intensive care unit (ICU) admissions, emergency department (ED) visits, and total hospital deaths. These

four of the six LAC medical centers were chosen because of their larger size and relatively more central location. The four medical centers provided daily counts data from July 1, 1999 to June 30, 2000 to serve as baseline information for the algorithms. ACDC received the data by facsimile or electronic mail according to the hospital data categories in Table 1.

Table 1. Categories of Data by Medical Center

Categories of data by medical center*			
LAC+USC	KDMC	Harbor	OVMC
Total hospital	Total hospital	Total hospital	Total hospital
Total ICU	Total ICU	Total ICU	Total ICU
Total deaths	Total deaths	Total deaths	Total deaths
General ED	Acute ED	Adult ED	
OB-GYN ED	Pediatric ED	Pediatric ED	
Pediatric ED	Psychiatric ED	Psychiatric ED	
Psychiatric ED			

* LAC+USC is Los Angeles County+University of Southern California Medical Center, KDMC is Martin Luther King/Drew Medical Center, Harbor is Harbor/UCLA Medical Center, and OVMC is Olive View Medical Center.

Data Management

Using Microsoft Excel, ACDC developed a database that would organize the data and automatically perform statistical calculations and provide graphical output. The data were transferred or manually entered into the database on a daily basis. In order to quickly focus on Total hospital, Total ICU, Total deaths, and Total ED data, the category of Total ED was made by combining the counts of all EDs.

The Algorithms

The outbreak detection algorithms included those used by the CDC in the *Morbidity and Mortality Weekly Report (MMWR)*, the Current Day (CD) method used by the World Health Organization to identify meningococcal meningitis outbreaks, the Current-Previous method used by the Oregon State Health Department, and the CuSum method, also known as the Salmonella Outbreak Detection Algorithm (SODA) used by CDC. These algorithms were modified to analyze daily data instead of weekly data and to explore different levels of "sensitivity" by varying the lengths of reference periods.

Figure 1. Calculation of MMWR algorithm.

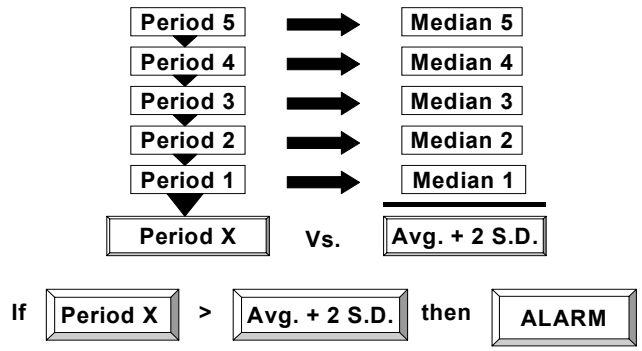
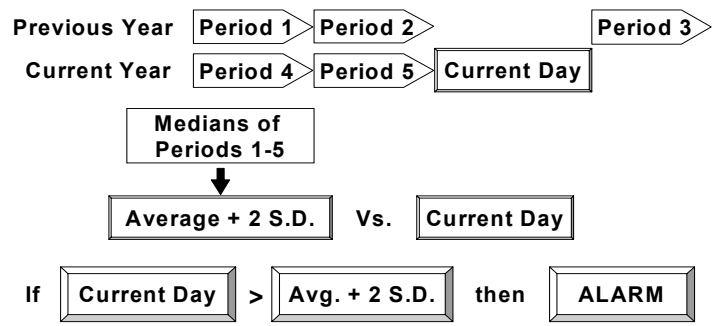


Figure 2. Calculation of Current-Previous algorithm.



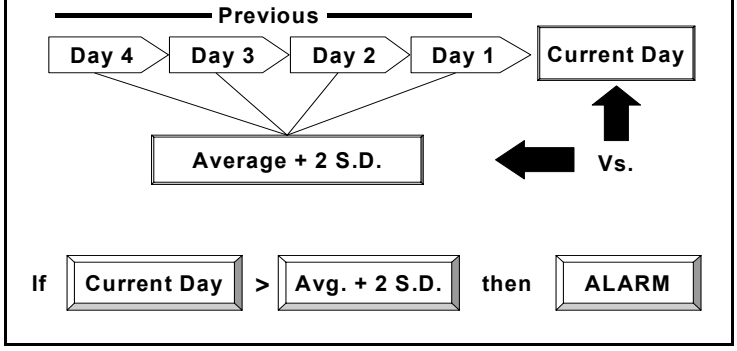
The *MMWR* method used the medians of the counts for five previous periods centered on days of the same name as the current day of interest to find an average (Figure 1). This average plus two standard deviations served as the reference value to which the count for the day of interest was compared. The algorithm triggered an alarm when the count for the day of interest exceeded the reference value. The authors developed two versions of this algorithm. The first version, designated MMWR3, referenced a three-day time period, and the second, designated MMWR7, referenced a seven-day time period. For example, in applying MMWR3 to a Monday (Period X in Figure 1), the medians of the daily counts of the five previous three-day sets of Sunday, Monday, and Tuesday would be used to calculate an average. The addition of two standard deviations to the average would define a reference value that would be compared to the count for the current Monday. The investigators modified this algorithm to account for certain weekdays being busier than others in terms of admissions and visits.

The Current-Previous algorithm averaged the medians of the daily counts of five time periods (Figure 2). To account for seasonality, the first three time periods were of the previous year. The two versions of this algorithm were designated CP3 and CP7. CP3 referenced a time period of three days and CP7 referenced a time period of seven days. For example (Figure 2), using the three-day version of this algorithm, the authors would define Period 5 as the three days before the day of interest, Period 4 as the three days before Period 5, Period 1 as the same calendar days as Period 4 but of the previous year, Period 2 as the same calendar days of Period 5 but of the previous year, and Period 3 as the three calendar days after the current day of interest but of the previous year. The medians of the daily counts of these five three-day periods would be averaged.

The average plus two standard deviations made the reference value which would be compared to the count for the day of interest. When the count for the day of interest exceeded the reference value, the algorithm triggered an alarm.

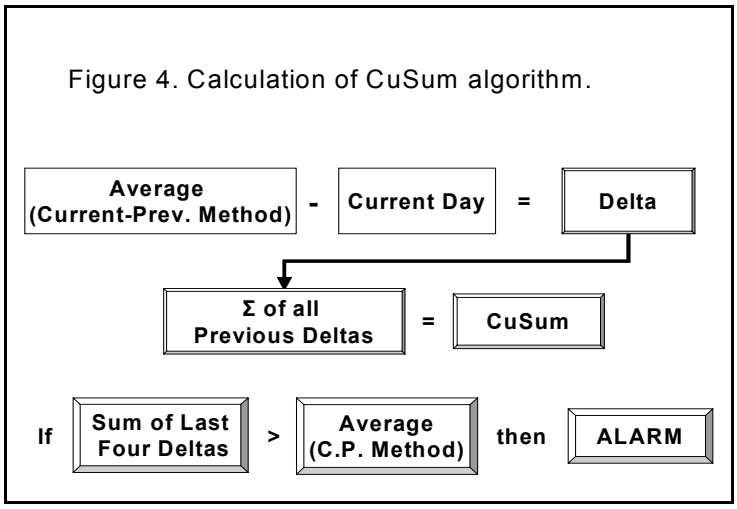
The Current-Day (CD) method compared an average of the daily counts of the previous four days plus two standard deviations to the count of the day of interest. When the count for the day of interest was greater, the algorithm triggered an alarm (Figure 3).

Figure 3. Calculation of Current Day algorithm.



There were three-day, seven-day, and fourteen-day versions of the CuSums method. The reference value of the CuSums method was calculated exactly like the reference value in the Current-Previous method but did not include the addition of two standard deviations. The difference between the CuSum reference value and the count for the day of interest provided a value designated *delta*. The cumulative sum of the *deltas* was the CuSum. The sum of the deltas of the day of interest and the previous three days was compared to the reference value. When the sum of the four deltas exceeded the reference value, the algorithm triggered an alarm (Figure 4). A line graph of the CuSums provided a sensitive visual tool of trends as positive slopes indicated increases in admissions, visits, and deaths. Alarms from the CuSum algorithms were considered as secondary alarms because they tended to alarm or not alarm for extended periods of time. In other words, the CuSum alarms tended to cluster.

Figure 4. Calculation of CuSum algorithm.



Surveillance

The first step of looking at the alarms involved a daily summary of the total alarms in each medical

center. For example, if the current date is December 12, 2000, the number of total alarms and the number of alarms within each hospital data category would be reviewed as shown in Table 2. The medical centers with any alarms would receive closer review. In the example, LAC-USC was the only medical center with alarms.

Table 2. Example of Daily Summary of Alarms by Medical Center

Current date: 12/12/2000

		Number of alarms by hospital data category			
Medical center*	Total Alarms	Hospital admissions	ICU admissions	Total deaths	Total ED
Harbor	0	0	0	0	0
LAC-USC	12	0	6	4	2
KDMC	0	0	0	0	0
OVMC	0	0	0	0	N/A

* LAC+USC is Los Angeles County-University of Southern California Medical Center, KDMC is Martin Luther King/Drew Medical Center, Harbor is Harbor/UCLA Medical Center, and OVMC is Olive View Medical Center.

The next step involved focusing on the medical centers with alarms and within each hospital data category comparing the number of previous alarms to the current number. To continue the example of December 12, 2000, Table 3 focuses on LAC+USC and shows that in the past two days there have been 11 and 12 total alarms but unlike the current day the majority of these occurred in hospital data categories other than the ICU. Since the majority of the alarms on December 12 occurred in the ICU, the next step would involve looking at this hospital data category.

Table 3. Example of Summary of One Medical Center by Hospital Data Category

Medical center: LAC-USC

			Number of alarms by hospital data category			
Date in 2000	Day of the week	Total Alarms	Hospital admissions	ICU admissions	Total deaths	Total ED
12/10	Sun	11	0	3	7	1
12/11	Mon	12	0	0	6	6
12/12	Tue	12	0	6	4	2
12/13	Wed	6	2	1	1	2
12/14	Thu	9	0	4	0	5
12/15	Fri	7	0	3	0	4

Table 4. Example of Summary of Hospital Data Category by Algorithm

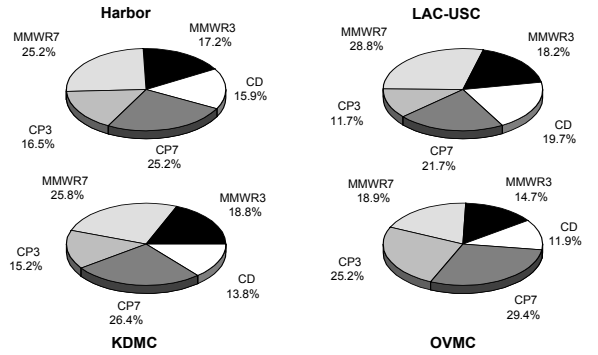
Hospital data category: ICU — Medical center: LAC-USC

	Algorithms that alarmed								
	MMWR		Current-Preveious		Current Day	CuSums			
Date in 2000	3	7	3	7		3	7	14	Total alarms
12/10						X	X	X	3
12/11									0
12/12	X	X		X		X	X	X	6
12/13							X		1
12/14	X	X		X			X		4
12/15						X	X	X	3

Seeing which algorithms caused certain hospital data categories to have relatively more alarms would be the next step in surveillance. Each algorithm refers to a particular time period and so several algorithms triggering alarms should warn the investigators that an unusual increase has occurred. Continuing the example of December 12, 2000, Table 4 shows MMWR3, MMWR7, and CP7 triggering alarms for the first time since two days earlier. The total number of alarms for the previous seven days, month, and three months would be graphed with a vertical bar chart (data not shown) to give the investigators more perspective on the current day's alarms.

RESULTS

Figure 5. Percent of Alarms by Algorithm, 7/1/00-9/6/00.



LAC-USC continued to provide daily count data into the year 2001; however, the other medical centers did not. OVMC stopped providing data on September 6, Harbor stopped on November 30, and KDMC stopped on December 4.

From July 1, 2000 to September 6, 2000, MMWR7 and CP7 usually triggered the most alarms (Figure 5). Regarding Total hospital (hospital admissions) data, OVMC experienced the greatest number of alarms, 38, while Harbor experienced 26 alarms, and LAC-USC and KDMC each had 12. Regarding ICU data, OVMC experienced 80 alarms, while LAC-USC experienced 44, Harbor 35, and KDMC 26. Regarding Total deaths data, Harbor experienced 49 alarms, while KDMC experienced 34, LAC-USC 31, and OVMC 25. Regarding Total ED visits, Harbor experienced 26 alarms, LAC-USC 22, and KDMC 21 (OVMC did not have this hospital data category).

DISCUSSION

The intended purpose of this surveillance system was to detect unusual increases in hospital admissions, ED visits, ICU admissions, and hospital deaths that might indicate an unsuspecting population's exposure to a bioterrorist weapon or a naturally occurring infectious disease. Unfortunately, the surveillance system lost participants after the DNC ended and after the Associate Director of Clinical and Medical Affairs left his LAC position. One of the misconceptions that might have contributed to the drop in participation was that the threat of bioterrorism is only real during large national or international gatherings like the DNC or the Olympics. A surveillance system with set protocols for easy and efficient maintenance can only be established when government officials (local, state, and national) realize that bioterrorism has a potential to occur at any time and affect large populations for an extended period.

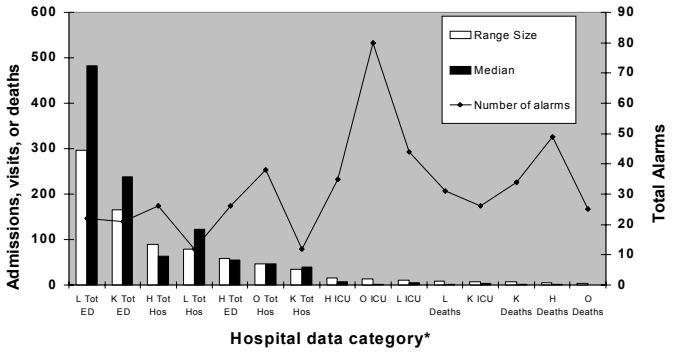
Although one of the purposes of this study was to validate the modified algorithms, the lack of any protocols to do this left the questions of predictive value positive and negative unanswered. In other words, how often the algorithms alarmed when outbreaks of community illness occurred and how often they did not alarm when possibilities of common-source community illness were absent were not measured. Certain algorithms triggered more alarms than others. However, this should not be interpreted that these algorithms are more sensitive and more useful than others. The investigators used several algorithms because the alarms might indicate not just outbreaks, but various unrelated illnesses, hospital-specific practices, random variation, or low baseline data. One method of validation could involve collecting diagnostic or admission data with chief complaints. However, any method of validation most probably would require hospital staff to collect the data.

A related limitation of the surveillance system was the lack of protocols for investigation at the medical center. When algorithms alarmed, there were no established procedures that stated who would investigate and what the investigation would entail. Access to diagnostic data or chief complaint data at admission could help assess the presence of any common exposures or risk factors.

Part of the problem in establishing investigation protocols was the one-day delay (three-day delay for Mondays) in receiving the data. The earliest the alarms could trigger was one day after the medical centers attended to their patients. In the case of bioterrorist events, this delay might be crucial to saving many lives. Furthermore, the one-day delay often increased as most of the medical centers did not have a consolidated database and collected the daily counts by hand tallies in some instances. Thus, the busyness of one department may delay the daily count data from being transmitted. Indeed, the method of facsimile and E-mail dictated a data management system requiring a large amount of manual entry and daily updating of data analysis programs at ACDC. The necessity of such tasks hurt the authors' ability to establish and coordinate any investigative efforts at the medical centers.

The size of the medical center and its facilities for the various categories of hospital data could have played a role in the number of alarms that triggered. As one might have expected, hospital data categories with low numbers of daily counts and small ranges of values demonstrated a greater potential for alarms to trigger (Figure 6). For example, from July 1, 2000 to September 6, 2000, total hospital deaths in Harbor had a median daily count of one, a range of zero to five deaths in a day, and the

Figure 6. Ranges and Medians of Daily Counts by Number of Alarms, 7/1/00-9/6/00.



* L =LAC-USC, K=KDMC, H=Harbor, O=OVMC

second largest number of alarms among all hospital data categories (49 alarms). Some of these hospital data categories had periods where a majority of the algorithms triggered alarms. Investigation of alarms might help determine thresholds and guidelines that would increase the predictive values of the surveillance system.

With respect to the surveillance conducted by the collaboration of ACDC, CDC, and the California State Health Department, the surveillance conducted here was established and maintained by one epidemiologist and one student worker. Thus, this surveillance system is relatively cost-effective. Although the modifications of established disease outbreak algorithms seem to work with the study data, the question of validity remains. Answering this question requires close collaborations with medical centers.

RECOMMENDATION

To evaluate the usefulness of this surveillance system and improve it, a formal relationship between ACDC and any participating medical center needs to be established such that standard protocols are defined and followed for investigating causes of alarms. ACDC and medical centers need to collaborate in developing databases that allow for real-time or near real-time transmission of data. Again, the lack of centralized databases in medical centers contributes to the delay in ACDC getting information. In addition, chief complaint and diagnostic data at time of observation of admission, visit, and death could only help to quickly evaluate the algorithms. This evaluation could suggest the need to modify the algorithms further to improve predictive values.

DEMOCRATIC NATIONAL CONVENTION - BIOTERRORISM SYNDROMIC SURVEILLANCE

Domestic threats of bioterrorism cannot be ignored. Advances in technology allow terrorists to disseminate bioterrorist agents, while at the same time the public has become more aware of bioterrorism. Effective public health response to a bioterrorist event needs timely surveillance because after such an event there may be only a short window of opportunity, sometimes only hours or days, to provide treatment, prophylaxis, or implement other control measures.

Traditionally, disease surveillance by public health is done by following reports of confirmed cases of disease. However, this surveillance may not be timely enough to allow for effective public health response after a bioterrorist attack.

Syndromic surveillance follows reports of clinical symptoms before confirmed diagnoses are made. An increase in syndrome reporting may be an indicator of an increase in disease which can immediately lead to an epidemiologic investigation.

Since high-profile gatherings of people may be targets of bioterrorist attacks, the Centers for Disease Control and Prevention (CDC), with the Acute Communicable Disease Control Unit of the Los Angeles County (LAC) Department of Health Services, developed a short-term syndromic surveillance project for the Democratic National Convention held in Los Angeles in August 2000. The project, called the Democratic National Convention-Enhanced Surveillance Project (DNC-ESP), was modeled on a joint short-term surveillance project of the CDC and Seattle and King County Public Health that was used for the World Trade Organization meeting in December 1999.

The main objective of the DNC-ESP was timely detection of a bioterrorist event or other infectious disease outbreak using syndromic surveillance of patients presenting to emergency departments in LAC. A long-term objective was the development of partnerships with non-traditional surveillance sources.

After preliminary discussions in April 2000, during May through July, local, state, and CDC personnel recruited hospital emergency departments to be the surveillance sites. Project personnel trained emergency department staff in the implementation of the project in early August.

Although the DNC was only 4 days long from August 14-17, the surveillance period stretched from August 7-22 to allow for data collection before the DNC to establish baseline disease reporting. The surveillance period continued for 5 days after the DNC to cover the most common incubation periods for bioterrorist agents.

METHODS

We approached 11 hospital emergency departments and an airport clinic to be part of the project and all agreed. We chose both community and academic hospitals to capture a broad range of

the population, and selected emergency departments that were geographically dispersed throughout LAC but were close to the DNC convention site or to DNC delegate hotels.

Several critical bioterrorism agents selected for syndromic surveillance included anthrax, tularemia, plague, smallpox, viral hemorrhagic fevers, botulism, and various other potential threats. Seven clinical syndromes were chosen to represent the clinical manifestations of these bioterrorism agents: respiratory infection with fever, rash with fever, sepsis or non-traumatic shock, diarrhea/gastroenteritis, meningitis/encephalitis, botulism-like syndrome, or unexplained death with history of fever. The last three were designated rare syndromes based on past surveillance experience.

A form was attached to the chart of each patient upon registration to the emergency department (ED) and the following information was collected: age, gender, if the patient had any connection to the DNC (loosely defined to include being a delegate, journalist, protester, first responder, etc), and the date and time of registration to the ED. After evaluating the patient, the health care provider would check off a box on the form with one of the 7 clinical syndromes under surveillance or a box “all other syndromes.”

Hospital personnel were asked to enter data from the forms as soon as possible after the doctor evaluated the patient. The data were submitted to a database on a secure internet site where an automatic date/time stamp was placed on the data upon receipt.

DATA ANALYSIS

The data were monitored hourly from 8:00 AM to 5:00 PM Monday through Friday and every four hours between 6:00 PM and 8:00 AM and on the weekends. The data were monitored visually for overall trends in syndrome reporting and for individual reports of any of the three rare syndromes. At 10:00 AM daily, all data were downloaded from the database and quantitatively analyzed by outbreak detection methods.

For the traditional outbreak detection method, we used 2 by 2 tables to detect an increase or unusual activity in syndrome reporting. We calculated prevalence ratios of individual syndromes by comparing the proportion of reports received in the previous 24 hours of a given syndrome to the proportion of reports received of that syndrome in all the other days combined. We did this everyday, for each syndrome, by hospital and by all hospitals combined. We used chi-square tests of significance in our calculations.

ACTIONS TAKEN

We followed up on the data in 3 ways:
Individual reports of the rare syndromes (meningitis/encephalitis, botulism-like syndrome and unexplained death) were immediately followed up with a telephone call to the ED. We investigated

selected statistically significant increases of syndrome prevalence ratios with visits to the hospitals and chart review. Finally, we faxed daily reports to each hospital of the number of patient visits reported to us and their syndromes.

EVALUATION

We evaluated the DNC-ESP in three ways:
We calculated the timeliness of reporting by subtracting the date and time of patient ED registration from the date and time of the electronic submission of the data. We calculated the completeness of reporting by comparing the number of ED patient visits reported to us over the internet to the number of ED admissions recorded by the hospitals in their official records. Finally, we solicited feedback from emergency department directors with a structured survey.

RESULTS

Over the 16-day surveillance period, we received reports of 11,645 patient hospital visits, of which a total of 11,219 were unique. One hundred and forty-one visits, or 1.3%, were associated with the Democratic National Convention.

The overwhelming majority of visits to the ED were for “all other syndromes” (82.3%); only 6.7% were for the clinical syndromes under surveillance. No syndrome information was submitted for 11% of ED visits. The most common clinical syndromes reported were diarrhea/gastroenteritis (3.6% of the visits reported) and respiratory disease (2.2%). None of the other clinical syndromes accounted for more than one percent of ED visits.

We followed up on 2 cases of unexplained death, 2 cases of botulism-like syndrome, and 8 cases of meningitis/encephalitis. None of these cases were clustered in person, time, or place.

We recognized a total of 32 statistically significant increases in syndrome reports by the outbreak detection method. However, 16 of the 32 increases were due to reports of only 1-3 new cases of a given syndrome because the baseline incidence of disease reporting was so low for some of the syndromes. There were 10 increases due to 4-9 new reports, and 6 increases due to 10 or more new reports. We investigated 5 of the increases. None of the 5 investigations yielded evidence of an outbreak.

The median and mean time lag between admission time and date, and the time of electronic data submission was 14.3 and 21.6 hours, respectively. Sixty-nine percent of ED visits were reported.

Eleven of 12 ED directors responded to our survey. Ten of 11 felt that the DNC-ESP was a valuable tool to detect a potential bioterrorist attack and that participation in the project led to improved communication with public health that will continue into the future. All 11 would do it again if the threat of bioterrorism was increased in their community.

CONCLUSIONS

This was a successful joint CDC-LA County syndromic surveillance project. Reporting was timely compared to traditional surveillance methods. The project was comprehensive in terms of the number of hospitals involved, the number of different syndromes reported, and the completeness of reporting. However, it was time and resource intensive, and it required extensive preparation and the work of many people. No bioterrorist event or infectious disease outbreak was detected. Relationships with non-traditional surveillance partners were strengthened.

Future directions for syndromic surveillance include refinement of outbreak detection methods; refinement of the system so that it can be rapidly deployed in the event of a bioterrorist attack, and development of ongoing electronic data collection from EDs for routine syndromic surveillance.

EAST MEETS WEST: CAMPYLOBACTERIOSIS ASSOCIATED WITH AN ETHNIC SPECIALTY

BACKGROUND

Campylobacteriosis, the most common bacterial cause of foodborne illness in the United States, is spread via fecal/oral transmission. *Campylobacter* infections usually occur in single, sporadic cases and often are acquired by consumption of raw or undercooked meat or poultry. Outbreaks of campylobacteriosis can occur but usually are associated with drinking unpasteurized milk rather than consumption of raw or undercooked poultry . Recent studies have shown *Campylobacter* spp. may contaminate up to 80% of domestic retail raw chicken.[1]

During a routine case investigation, LAC DHS discovered that two unrelated but temporally associated campylobacteriosis cases consumed chicken dishes at a Japanese restaurant. In order to evaluate the association, LAC DHS initiated an investigation.

METHODS

Culture-confirmed campylobacteriosis cases with onsets from January 1, 1999 to December 31, 2000 were included in the study. Data was obtained from case history forms of reported campylobacteriosis cases and the LAC surveillance database.

LAC conducts passive surveillance for campylobacteriosis. After receiving a morbidity report of campylobacteriosis, Public Health Nurses (PHNs) interview the patient and complete the epidemiology case history form. These follow-up communications confirm the existence of a *Campylobacter* infection and collect and/or validate information regarding demographics, risk factors and other pertinent data. The completed case forms are reviewed and than entered into a surveillance database for each year. The surveillance database includes variables on demographics, serotype, restaurant exposure, certain risk factors, and a comment field. Information contained in the comment field includes suspicious or unusual information (including names of restaurants that are repeatedly mentioned).

Demographic characteristics (age, race/ethnicity, and gender), occupation, and risk factor (food consumed, travel history, etc.) information were summarized for each year separately and collectively for the study period. Proportional morbidity ratios, 95% confidence intervals (CIs), and Fisher exact p-values were calculated using Epi- Info. Population estimates were obtained from the 1999 Urban Research database.

RESULTS

During the study period 2,359 cases of campylobacteriosis were reported to LAC. Among these, 13 reported restaurant A exposure during the incubation period. These individuals were likely to

be Asian male students under the age of 30, and reporting student status as his/her occupation (Table 1). Asian race (RR=14, CI: 4.5-42, p<0.01) and the 20- to 24-year-old age group (RR=7.8, CI: 2.6-24, p<0.01) were associated with consuming undercooked chicken.

Table 1: 1999-2000 Campylobacteriosis Cases Who Ate at Restaurant A

Characteristic	Total Cases (n=13) No.	%
Gender		
Male	8	62
Female	5	38
Race		
Asian	8	62
White	4	31
Other	1	7
Age		
20-24	5	38
25-29	5	38
30+	3	24
Student		
Yes	6	46
No	7	54

All exposed cases consumed chicken prepared by the restaurant in traditional Japanese dishes. The restaurant serves two different chicken dishes that are purposely served undercooked. Tataki chicken is prepared by searing a small piece of chicken on a Japanese-style BBQ and served cold. Toriwasa chicken is prepared by placing small pieces of chicken in a saucepan of broth and bringing to a boil and then immediately cooking. The recipe calls for chicken in both dishes to be a desirable internal color of "pink to red." The chicken used in both dishes was purchased from a custom slaughterhouse and transported to the restaurant in an unsanitized ice chest.

DISCUSSION

Ethnic delicacies from a particular restaurant were associated with campylobacteriosis. Restaurants are rarely identified as the source for *Campylobacter* infections. During the study period LAC identified 3 other restaurant-associated campylobacteriosis outbreaks where chicken was identified as the suspected source.

Previous studies have shown that most retail raw chicken is contaminated with *Campylobacter* spp.

One study reported an isolation rate of 98%[1] and a California study in the 1980s discovered that 68% of retail chickens were contaminated.[2] In 1999, LAC DHS performed a convenience sample of retail whole raw chickens and found that 19 of 30 chickens (63%) were positive for *Campylobacter* species.

Asian race/ethnicity, the age group of 20 to 24 years old, and student status were associated with consumption of raw/undercooked chicken. Anecdotal information from interviews of Japanese students indicated that the perceived risk of disease acquisition was low. Additionally, foreign- born Asian cases believe that chickens are "clean" in Japan. However, a recent Japanese study reported that 46% of Japan's retail chicken was contaminated with *Campylobacter jejuni*.[3]

The 2000 California Uniform Retail Food Facilities Law (CURFFL) states that chicken shall be heated to a minimum internal temperature of 165 F. There are two exceptions to the law: (1) the consumer can specifically order a food item less cooked, or (2) the food facility must notify the consumer orally or in writing that he/she has ordered a raw or less than thoroughly cooked food item. If exceptions are met, the food facility can serve undercooked or raw food items.

RECOMMENDATIONS

CURFFL exists to protect the consumer from unsafe foodhandling practices. Appropriate enforcement agencies need to enforce the law. Additionally, we can educate the public of the risks of consuming raw/undercooked meat or poultry by placing food warning labels in the restaurant or on the menu. Public health departments should be alert for ethnic foods which may be high risk (steak tartare, cured meats, etc.) during routine inspection or investigation of foodborne illness in restaurants. Health departments should establish communication with ethnic restaurants and food associations through public health newsletters and other outreach methods. These relationships can be used to educate specific communities about the consequences of consuming high-risk foods.

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EXPANDED KINDERGARTEN RETROSPECTIVE SURVEY, 1996 AND 1999

BACKGROUND

During the 1995-1996 school year, more than 160,000 children entered kindergarten in Los Angeles County (LAC). During the 1998-1999 school year, the number of children entering kindergarten in LAC was more than 150,000 children. California law requires that proof of vaccination, or exemption from vaccination, be presented to the school staff before a child can be admitted to any public or private California school.[1] Children who have not received all the vaccinations required for school entry must obtain them before being admitted. A child lacking two or more doses in a series of vaccinations may be admitted to school on the condition that the additional doses are received as they become due in the future. Exemptions from vaccination can be granted for medical reasons, or religious or personal beliefs.

To monitor vaccination coverage levels among preschool-aged children in LAC, the Immunization Program (IP) reviews vaccination records for vaccine dates for a sample of kindergarten entrants each year. In 1996 and 1999 the IP reviewed all vaccination records for all kindergarteners entering over 46 LAC schools during the 1995-1996 and 1998-1999 school years. The results of the 1996 and 1999 Expanded Kindergarten Retrospective Surveys (EKRS) are presented in this report.

The Kindergarten Retrospective Survey is a historical cohort survey. The vaccination dates from the school vaccination record are used to retrospectively estimate vaccination coverage levels during prior years and calculate age-appropriate series completion rates. In 1996 and 1999 an EKRS was conducted. The 61,268 children who entered a kindergarten in the Los Angeles Unified School District (LAUSD) in 1995 were eligible for inclusion in the 1996 EKRS. The 59,992 children who entered a kindergarten in the LAUSD in 1998 were eligible for inclusion in the 1999 EKRS. Most children who entered kindergarten during these school years were born in 1990 or 1993.

Age-appropriate coverage can be calculated at any desired age milestone. There, age-appropriate coverage levels are presented at 3, 5, 7, 12, 19, 24, 36, 48, and 60 months of age. Twenty-four months of age is a commonly used checkpoint for assessing age-appropriate vaccination coverage levels. In addition to calculating age-appropriate coverage, series completion rates were calculated for:

- one dose of poliovirus (OPV) vaccine and one dose of diphtheria and tetanus toxoids and pertussis (DTP) vaccine at 3 months of age
- two OPV and two DTP at 5 months of age
- two OPV and three DTP at 7 and 12 months of age
- three OPV, four DTP and one dose of measles-mumps-rubella (MMR) vaccine at 19, 24, 36, 48, and 60 months of age.

METHODS

In 1996, the LAC IP augmented the core KRS with an expanded survey by randomly selecting 49 additional public schools from the LAUSD. The selected schools represented 12% of the elementary schools in the LAUSD. The schools selected for the EKRS were not included in the core survey sample.

In 1999, the EKRS was repeated on 91 schools, including 46 of the 49 schools selected for the 1996 EKRS. At each selected school, a 100% sample of kindergarten student records was reviewed. In order to compare 1996 completion rates to 1999 completion rates, only information gathered from the mutual 46 schools were analyzed. There were 5,675 records in 1996 and 5,968 records in 1999.

RESULTS

Overall, 40% of the children in the 1996 EKRS sample had received four DTP, three OPV, and one MMR by 24 months of age (Table 1). At each age milestone assessed, coverage levels were generally lowest for Blacks and highest for Asians (Figure 1). At 3 month of age, 70% of Whites, 58% of Blacks, 69% of Hispanics, and 77% of Asians had received one OPV and one DTP. After 19 months of age, coverage levels gradually increased among all race/ethnic groups. At 60 months age, Asians had the highest coverage level at 80%. Hispanics had a 75% coverage level. Whites and Blacks had about the same coverage level at 60 months (67% and 66%, respectively).

In the 1999 EKRS sample, 55% of the children had received four DTP, three OPV, and one MMR by 24 months of age (Table 1). Similar to the 1996 results, coverage levels were generally lowest for Blacks and highest for Asians and Whites (Figure 2). At 3 months of age, 79% of Whites, 61% of Blacks, 74% of Hispanics, and 82% of Asians had received one OPV and one DTP. At 13 months of age, coverage levels for two OPV and three DTP were about the same as the coverage levels at 3 months of age for each race/ethnic group. Coverage levels were lowest for Blacks and Hispanics at 7 months: 29% for Blacks and 41% for Hispanics. Asians and whites experienced their lowest coverage level at 19 months of age: 48% for Asians and 50% for Whites. After 19 months of age, coverage levels gradually increased among all race/ethnic groups. At 60 months of age, Asians, Hispanics, and Whites had the highest coverage levels at 90%, 89%, and 88%, respectively. Blacks had the lowest coverage level of 80%.

Estimates for both the 1996 and 1999 EKRS were summarized by Service Planning Areas (SPAs) (Table 2, Figure 3). SPAs with at least 30 students residing in them were included in the analysis (Figures 4 & 5). In the 1996 EKRS coverage levels for four DTP, three OPV, and one MMR at 24 months of age ranged from 33% to 60%. In the 1999 EKRS coverage levels at 24 months of age ranged from 45% to 60%.

Similarly, estimates for both surveys were summarized by zip code of the student's residence. Zip

codes with at least 30 students residing in them were included in the analysis. In 1996, coverage levels at 24 months of age for four DTP, three OPV, and one MMR from the 31 zip code areas included in the analysis ranged from 18% to 51% (Table 3). In 1999, coverage levels at 24 months for four DTP, three OPV, and one MMR from the 36 zip codes included in the analysis ranged from 0% to 74% (Table 4).

In the 1996 EKRS the coverage levels for hepatitis B vaccine were very low. At 24 months of age only 20 students (less than one percent of the total number of students included in the survey) had received three doses of hepatitis B vaccine. At 60 months of age 45 students had completed the hepatitis B vaccine series. However, this was still less than 1% of the total. In the 1999 EKRS 65% of all the students had received 3 doses of hepatitis B vaccine at 24 months of age. By 60 months of age the coverage level increased to 83%.

DISCUSSION

The EKRS provides a population-based estimate of vaccination coverage levels in children attending schools in the LAUSD. One limitation of a retrospective survey is that it measures events that happened in the past and does not provide a current estimate of vaccination coverage. The 1996 EKRS provides an estimate of vaccination coverage for children who were 24 months of age in 1992 while the 1999 EKRS provides an estimate of vaccination coverage for children who were 24 months of age in 1995.

In general, coverage levels have improved greatly between 1996 and 1999. Only SPA 5 experienced a drop in the overall coverage level. However, due to the small number of students from SPA 5, the change is probably not significant. The increase in hepatitis B coverage levels can be attributed primarily to the California law, effective August 1997, requiring three doses of the hepatitis B vaccine for school entry.[1]

Although the basic series of four DTP, three OPV, and one MMR should be completed by 18 months of age, many children in the surveys did not actually complete the basic series until kindergarten entry. Twenty-six percent of the children from the 1996 EKRS sample and 12% of the children from the 1999 EKRS sample were lacking one or more vaccinations at 60 months of age. Of the 161,638 children who entered kindergarten in LAC during the 1995-1996 school year, 92% provided documentation at the time of school entry that they had received the required vaccinations.[2] During the 1998-1999 school year, 91% of the 155,585 students provided documentation that they had received the required vaccinations.[3] The difference in coverage levels at 60 months of age and upon school entry indicate that many children are completing the basic series after their fifth birthday but before school starts.

A more timely estimate of vaccination coverage is provided by the National Immunization Survey (NIS) conducted by the Centers for Disease Control and Prevention. The NIS is an ongoing survey that provides estimates of vaccination coverage among children aged 19-35 months throughout

the United States and for selected urban areas. Data are collected quarterly by telephone using randomly selected telephone numbers. The estimated coverage from the NIS for four DTP, three OPV, and one MMR among children aged 19-35 months in LAC was 73% (±7%).[4] These data were collected in 1995 and represent children born between February 1992 and May 1994. This estimate is much higher than the coverage level of children 24 months old obtained from the 1999 EKRS, which generally represents children born in 1993.

There are several reasons for differences in coverage estimates from the EKRS and the NIS. First, the target age for the NIS is 19-35 months compared with 24 months for the EKRS. Children who were vaccinated according to the recommended schedule would complete the basic series of four DTP, three OPV, and one MMR by 18 months of age.[5] Series completion rates increase with age. By assessing vaccination coverage at 24 months of age, the EKRS allows six additional months for a child to complete the basic series. The NIS allows from one to up to 11 additional months for a child to complete the basic series. Second, the surveys collect information about different cohorts at different periods of time. The 1999 EKRS estimates vaccination coverage levels for children born in 1993 who were 24 months of age in 1995 whereas the 1995 NIS estimates coverage for children born between February 1992 and May 1994 and who were 19-35 months of age in 1995. Third, the NIS estimate for LAC is based on a sample of only about 440 respondents. Fourth, the NIS data are adjusted for households without telephones. The adjustment is based on national demographic characteristics that may not be applicable for LAC.[6] Lastly, the NIS takes a random sample of all children in LAC whereas the EKRS was a random sample of schools from the LAUSD. Therefore, the EKRS has limited representation from Antelope Valley, San Gabriel Valley and West Los Angeles. Also, children from private schools and other school districts are not represented in the EKRS.

Regardless of the survey method used, vaccination coverage level estimates for LAC are below the national goal to completely vaccinate 90% of children by their second year of life.[7] The IP will continue to monitor vaccination coverage estimates from various sources for use in the development of interventions and to improve vaccination coverage levels.

Table 1. Proportion of Kindergarten Students Who Received 4 DTP, 3 OPV, and MMR by 24 Months of Age, by Race/Ethnicity

	Expanded Survey Schools[a] 46 Schools, 1996			Expanded Survey Schools[b] 46 Schools, 1999		
Race/ Ethnicity	Sample size	% of sample	% up-to-date	Sample size	% of sample	% up-to-date[b]
White	538	9.5%	36.1%	344	5.8%	64.8%
Black	379	6.7%	31.9%	229	3.8%	38.4%
Hispanic	4,475	78.9%	41.2%	4,640	77.8%	55.0%
Asian	141	2.5%	50.4%	165	2.8%	61.2%
Total	**5,675[c]**	**100.0%**	**40.1%**	**5,968[d]**	**100.0%**	**54.8%**

a. Random sample of LAUSD public elementary schools. In 1996, the sampled schools represented 12% of the elementary schools in the LAUSD. At each school, records for all kindergarten students were reviewed.
b. The same LAUSD schools that were assessed in 1996 were assessed in 1999.
c. Total includes 142 (2.5%) children of other or unknown race/ethnicity.
d. Total includes 590 (9.9%) children of other or unknown race/ethnicity.

Table 2. Proportion of Kindergarten Students Who Received 4 DTP, 3 OPV, AND MMR BY 24 Months of Age, by SPA

SPA[c]	Expanded Survey Schools[a] 46 Schools, 1996			Expanded Survey Schools[b] 46 Schools, 1999		
	Sample size	% of sample	% up-to-date	Sample size	% of sample	% up-to-date[b]
2: San Fernando	1,441	25.4%	37.8%	1,591	26.7%	60%
4: Metro	2,157	38.0%	45.1%	2,656	44.5%	55%
5: West	35	0.6%	60.0%	41	0.7%	51%
6: South	535	9.4%	33.1%	297	5.0%	45%
7: East	862	15.2%	40.4%	938	15.7%	51%
8: South Bay	251	4.4%	33.1%	212	3.6%	49%
Total	**5,675**[d]	**100.0%**	**40.1%**	**5,968**[e]	**100.0%**	**54.8%**

a. Random sample of LAUSD public elementary schools. In 1996, the sampled schools represented 12% of the elementary schools in the LAUSD. At each school, records for all kindergarten students were reviewed.
b. The same LAUSD schools that were assessed in 1996 were assessed in 1999.
c. SPA=Service Planning Area. Analysis excludes SPAs with less than 30 records and records with missing SPA information.
d. Total includes 394 (6.9%) children from SPA 1 or with missing SPA information.
e. Total includes 233 (3.9%) children from SPAs 1 & 3 or with missing SPA information.

Table 3. Proportion of Kindergarten Students Who Received 4 DTP, 3 OPV, and 1 MMR by 24 Months of Age, by Zip Code of Residence, 1996

Coverage Estimate Ranges for Zip Codes of Residence				
10%-19%	**20%-29%**	**30%-39%**	**40%-49%**	**50%-59%**
90247	90027	90003	90005	90004
	90255	90008	90006	91406
	91343	90018	90012	
	91401	90028	90022	
		90047	90026	
		90303	90032	
		90731	90042	
		91335	90057	
		91606	90201	
			90270	
			90280	
			91304	
			91331	
			91340	
			91411	

Table 4. Proportion of Kindergarten Students Who Received 4 DTP, 3 OPV, and 1 MMR by 24 Months of Age, by Zip Code of Residence, 1999

Coverage Estimate Ranges for Zip Codes of Residence					
0%-9%	**20%-29%**	**40%-49%**	**50%-59%**	**60%-69%**	**70%-79%**
90022	90247	90008	90005	90017	91304
		90012	90006	90026	91307
		90018	90020	90028	
		90027	90033	91335	
		90032	90043	91340	
		90042	90057	91343	
			90069	91606	
			90201		
			90255		
			90270		
			90280		
			90731		
			91306		
			91331		
			91356		
			91401		
			91402		
			91406		
			91411		

**Figure 1. 1996 Expanded Kindergarten Retrospective Survey
Proportion Up-to-date at Selected Ages by Race
n=46 schools; 5,675 students**

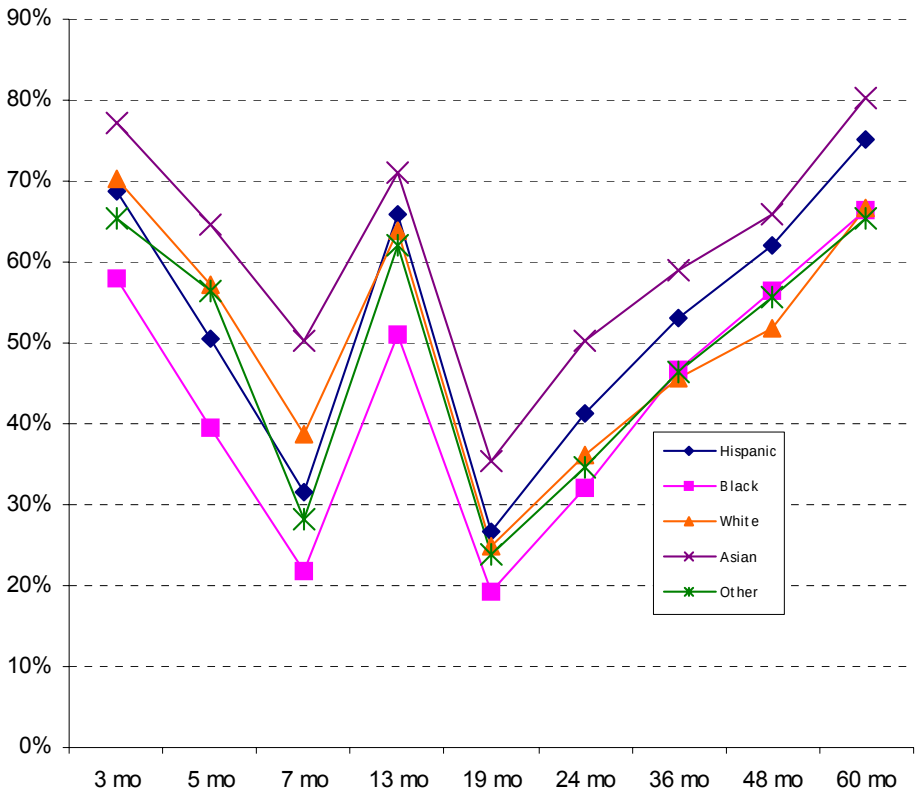


**Figure 2. 1999 Expanded Kindergarten Retrospective Survey
Proportion Up-to-date at Selected Ages by Race
n=46 schools; 5,968 students**

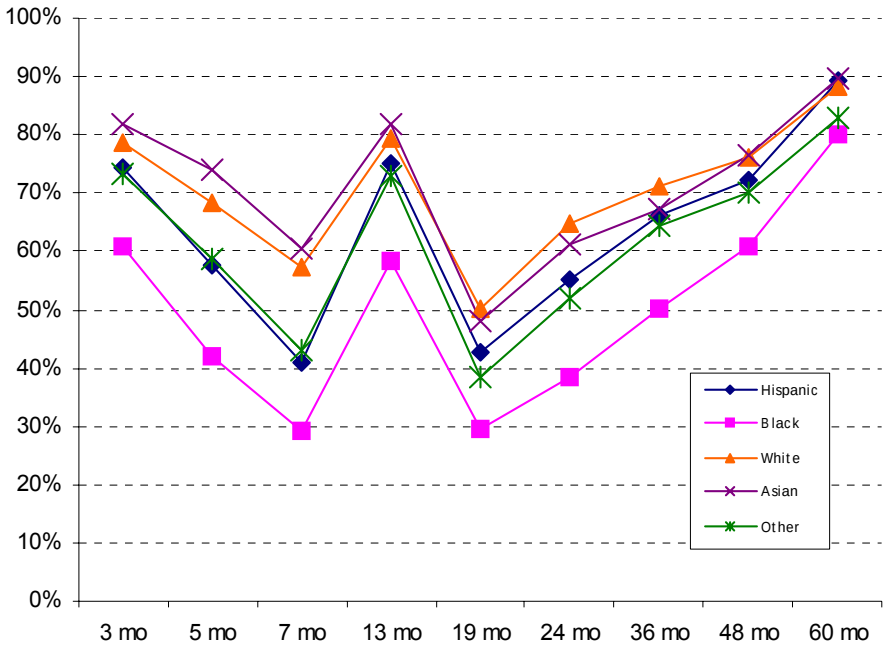


Figure 3. Proportion of Kindergarten Students Who Received 4 DTP, 3 OPV, and 1 MMR by 24 Months of Age, By Service Planning Area (1996/1999)

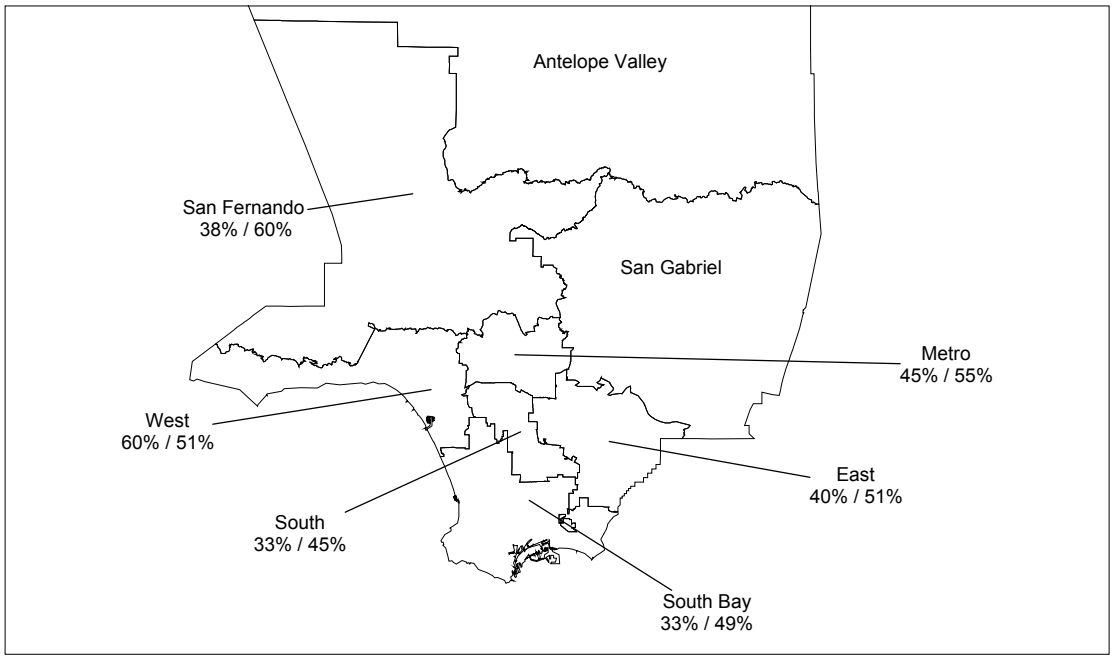


**Figure 4. 1996 Expanded Kindergarten Retrospective Survey
Proportion Up-to-date at Selected Ages by SPA
n=46 schools; 5,675 students**

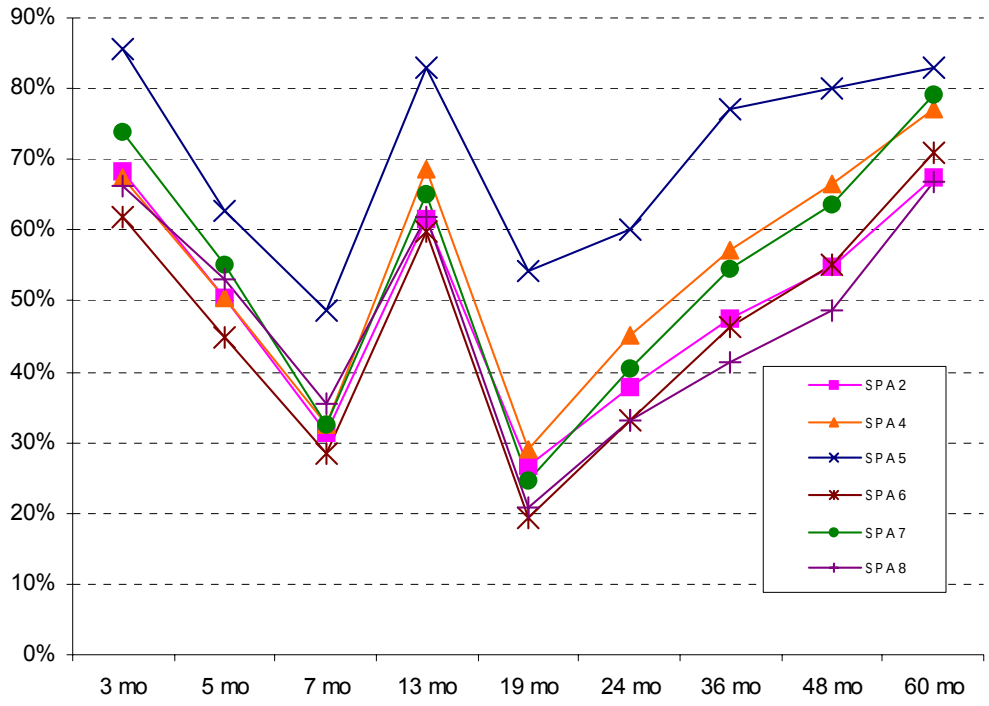
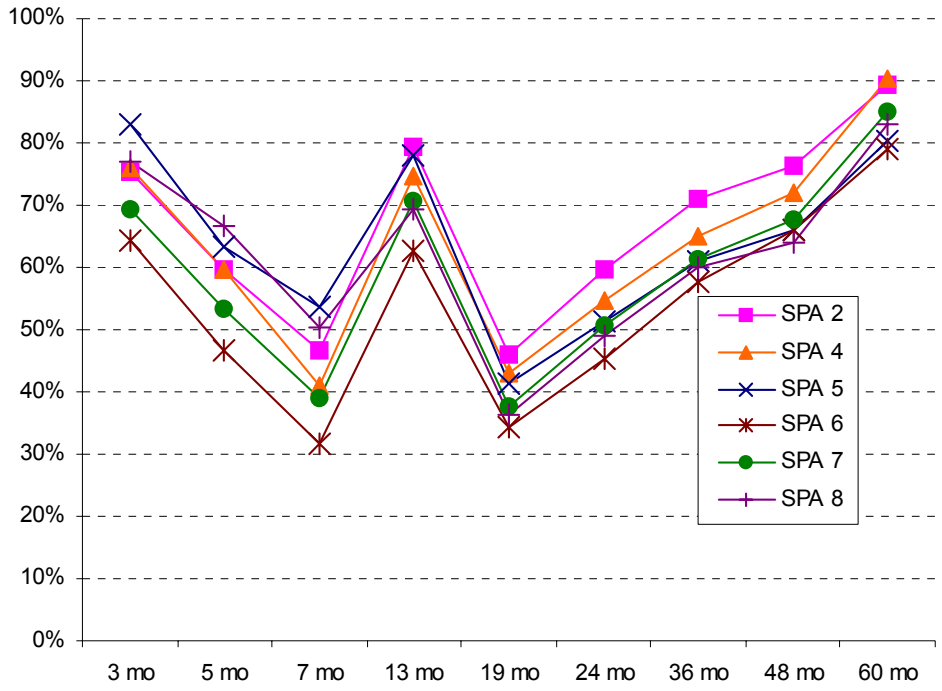


Figure 5. 1999 Expanded Kindergarten Retrospective Survey
Proportion Up-to-date at Selected Ages by SPA
n=46 schools; 5,968 students



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FACTORS ASSOCIATED WITH ACQUIRING PENICILLIN NONSUSCEPTIBLE INVASIVE PNEUMOCOCCAL DISEASE IN LOS ANGELES COUNTY

INTRODUCTION

In September 1995, the Los Angeles County (LAC) Department of Health Services initiated a laboratory and hospital infection control-based surveillance project for ten diseases and conditions including invasive pneumococcal disease (IPD), which is not a California state-reportable disease. Data showed that the annual incidence of reported IPD went from 8.4 cases in 1996 to 8.9 cases per 100,000 in 1999 and back down to 8.2 in 2000; the proportion of penicillin-resistant isolates increased from 19% to 29% and decreased to 24%, respectively in the same years. These findings are consistent with results from a recent 1997 study from seven metropolitan areas in the U.S. which showed that the proportion of penicillin-resistant isolates varied from 15% to 39%.[1]

This study examined risk factors associated with acquiring drug-resistant IPD for hospitalized LAC residents. The goal was to identify populations at risk for acquiring drug-resistant *S. pneumoniae* so strategies can be developed for prudent usage of antibiotics and efficient allocation of vaccine.

METHODS

The 1998 IPD surveillance data with antimicrobial susceptibility results (N=659) were merged with 1998 patient discharge data made available from the State of California Office of Statewide Health Planning and Development (OSHPD). Pneumococcal disease and underlying diseases were examined using codes as defined by the International Classification of Diseases, 9th Revision, Clinical Modification, U.S. Department of Health and Human Services, Washington D.C. (ICD-9-CM). The 1998 IPD surveillance data, which contained patient identifying information, were matched with OSHPD data by the facility name where the patient was hospitalized, age in years for date of birth, day of week, month and year of admission for admission date, and a truncated three-digit ZIP Code of residence.

A case-control study was performed. A case was defined as a LAC resident with a positive culture of penicillin-nonsusceptible (intermediate or high-level resistance) *S. pneumoniae* (PNSP) collected in 1998 from a normally sterile site and who was hospitalized at a LAC acute care hospital. A control was a hospitalized individual with a positive culture of penicillin-susceptible *S. pneumoniae* (PSSP) from a normally sterile site and collected in 1998.

Data were analyzed using Epi-Info 6.04 and SAS Version 6.12. A p-value of <0.05 was considered to be statistically significant. A map of cases and controls by place of residence was generated using MapInfo Version 3.0 software.

RESULTS

Forty-three percent (283) of the IPD surveillance cases were matched to the OSHPD data. When matched and unmatched IPD cases (N=376) were compared, there was no significant difference in gender (OR=0.93; CI: 0.67 to 1.28), culture site (OR=1.25; CI: 0.56 to 2.78), and rate of penicillin nonsusceptibility (OR=1.14; CI: 0.78 to 1.66) between the two groups. IPD cases less than 18 years were significantly less likely to be included in the study than adults over 18 years (OR=0.21; CI: 0.14 to 0.32).

In the study population (Table 1), 144 males and 139 females were aged 3 months to 99 years (mean $\pm$ SD, 55 $\pm$ 28 years). Whites constituted the majority of the patients (53%) followed by Blacks (17%) and Hispanics (16%). Forty-seven percent (134) were 65 years and over, 21% (59) were 45 to 64 years, 17% (48) were 15 to 44 years and 14% (39) were less then five years. *Streptococcus pneumoniae* was isolated from blood in 95% (269) of the patients, cerebral spinal fluid (CSF) in 4% (12), and other sterile sites in less than 1%, including one from joint/synovial fluid and one from chest fluid. The proportion of patients identified with isolates not susceptible to penicillin was 25% (72). Patients stayed in the hospital an average of nine days (s.d. $\pm$ 7). The majority of patients were admitted from home (92%) with an additional 14 patients referred from long-term care facilities. Seventy-four percent of the patients had one or more underlying medical conditions; the most frequent were pulmonary disease (38%), followed by cardiac disease (32%), malignancy (19%), and diabetes mellitus (15%). The most frequent expected source of payment for hospitalization reported were Medicare (42%), health maintenance organizations or preferred provider organizations (30%), and Medi-Cal or County Indigent Program (22%).

Seventy-two eligible cases with PNSP and 211 controls with PSSP were identified and compared. The cases did not differ significantly with respect to race/ethnicity, gender, and the other factors listed in (Table 2). Compared with controls, cases appeared to cluster geographically around the southwest portion of LAC (Map 1). Service Planning Area 5 (SPA 5) had the highest proportion of penicillin resistance for *S. pneumoniae* (45%), followed by SPA 4 (35%) and SPA 5 (27%).

Although the association between outcome and penicillin nonsusceptibility was not significant, more deaths occurred in the controls indicating that patients with PNSP were less likely to die then patients with PSSP (OR=0.85; CI: 0.38 to 1.86). Also, patients that were admitted with PNSP were less likely to have an underlying medical condition although the association was not significant (OR=0.89; CI:0.47 to 1.71). There was no difference in length of stay for cases and controls (Table 2).

Compared to PSSP patients, PNSP patients were significantly associated with being young and there was borderline significance with being very old. Patients who were 65 years and older and patients less than 18 years old were more likely than patients 18-64 years to be diagnosed with penicillin nonsusceptibility (OR=1.83, 95% CI: 0.94 to 3.58 and OR=2.57, 95% CI: 1.07 to 6.19) (Table 2). In addition, among those 60 years and over, PNSP cases were not significantly more

likely than controls to have been admitted from a long-term care facility versus from home (OR=1.07; 95% CI: 0.23 to 4.04).

DISCUSSION

ACDC identified four important findings regarding penicillin nonsusceptible IPD in LAC:
(1) nonsusceptibility occurred in 25% of the patients, (2) nonsusceptibility varied by SPA, (3) nonsusceptibility was associated with patients less than 18 and older than 65 years, and (4) nonsusceptibility was not associated with increased mortality.

Zangwill et al. published the most recent study assessing IPD and penicillin nonsusceptibility in LAC.[13] They examined three years of data (April 1992 to March 1995) from the Kaiser Permanente Southern California Region (health maintenance organization) that included LAC and seven other contiguous counties. In their population-based study, they found 14% penicillin nonsusceptibility. The health department's surveillance system for IPD, which include inpatients and outpatients, observed annual penicillin nonsusceptibility rates that fluctuated from 20%, 29%, and 24% in 1996, 1999, and 2000. Our study examined only hospitalized cases and determined that the proportion of hospitalized patients with PNSP (25%) was not substantially different from what was observed for all the cases reported in 1998 to the IPD surveillance system in 1998 (24%). The trend of increasing resistance toward penicillin in LAC appears to have almost doubled from what was first reported by Zangwill. In a study of 34 medical centers throughout the U.S. in 1998, the rate of resistance to penicillin was 29.5%, which is slightly higher than the rate we observed.[3]

Numerous studies have identified children less than five years and adults over 65 years at a higher risk for penicillin nonsusceptibility.[5,6,9] Risk factors for penicillin resistance have often been associated with extremes of age. Studies have recognized exposure to a day care center,[7] exposure to a long-term care facility,[6] and underlying medical condition[9] as risk factors for PNSP. In this study, PNSP cases were not associated with exposure to a long-term care facility or the presence of an underlying condition although the numbers were small for the former. No data on day care exposure were obtained for this study. Other factors elucidating the mechanisms for the increased incidence of penicillin resistance in the very young and old in LAC will have to be studied.

Some limitations of the OSHPD data may have affected the conclusions drawn in this study. First of all, matching cases in the IPD surveillance and OSHPD data were difficult because OSHPD data were incomplete for confidentiality purposes (no date of birth, truncated ZIP code, etc.). Also, there was a potential for miscoding in the OSHPD data. Problems with misclassifying diagnosis codes may have occurred with underlying medical condition. It is unknown whether there was coding variation between hospitals. Other studies that recovered their data directly from reviewing medical records found an association between penicillin resistance and underlying condition. Our study relied heavily on the OSHPD data, which may have contributed to not finding a difference with regard to underlying medical condition. Also, persons under 18 years old were less likely to be included in the study. This could be a consequence of using OSHPD data because children are

hospitalized less frequently and have fewer underlying medical conditions that could complicate their illness. In addition, known risk factors such as previous antibiotic usage[2,4,8-10] and prior hospitalization[12] were not available in the OSHPD data. Further studies are needed to determine whether these same risk factors are associated with penicillin nonsusceptibility in LAC.

The overall mortality in this study was 17%, which is consistent with findings from other studies.[5,6,11] Mortality appeared to be less in PNSP patients than with PSSP patients (15% vs. 18%) but the association was not significant. The role of drug resistance for IPD on mortality remains unclear. Most studies of IPD have not demonstrated an association between antibiotic resistance and increased mortality. Turett et al.[11] were the first to report penicillin resistance as an independent predictor of mortality among hospitalized patients with pneumococcal bacteremia. It should be noted that half of the cases in Turett's study had human immunodeficiency virus (HIV) infection whereas in this study 2% were infected with HIV. Further study is needed. Although not supported by our study, if penicillin resistance is a predicator of mortality, it lends support for targeting groups who are at high risk for acquiring drug-resistant IPD for vaccination because of increased probability of poor clinical outcome.

With the widespread overuse of antibiotics, the problem of microbial drug resistance will continue to increase as a major public health threat. It is through educational programs targeting the community and medical establishment about proper antibiotic usage that we must attempt to reduce the growing numbers of drug-resistant pathogens. In addition, vaccination campaigns utilizing the recently Food and Drug Administration-approved pneumococcal conjugate vaccine for very young children and the pneumococcal polysaccharide vaccine for the elderly and high-risk individuals must be utilized to decrease the incidence of those at high risk for not only penicillin resistance but also IPD.

TABLE 1: Demographic Statistics of Hospitalized Cases of IPD, LAC, 1998 (N = 283)

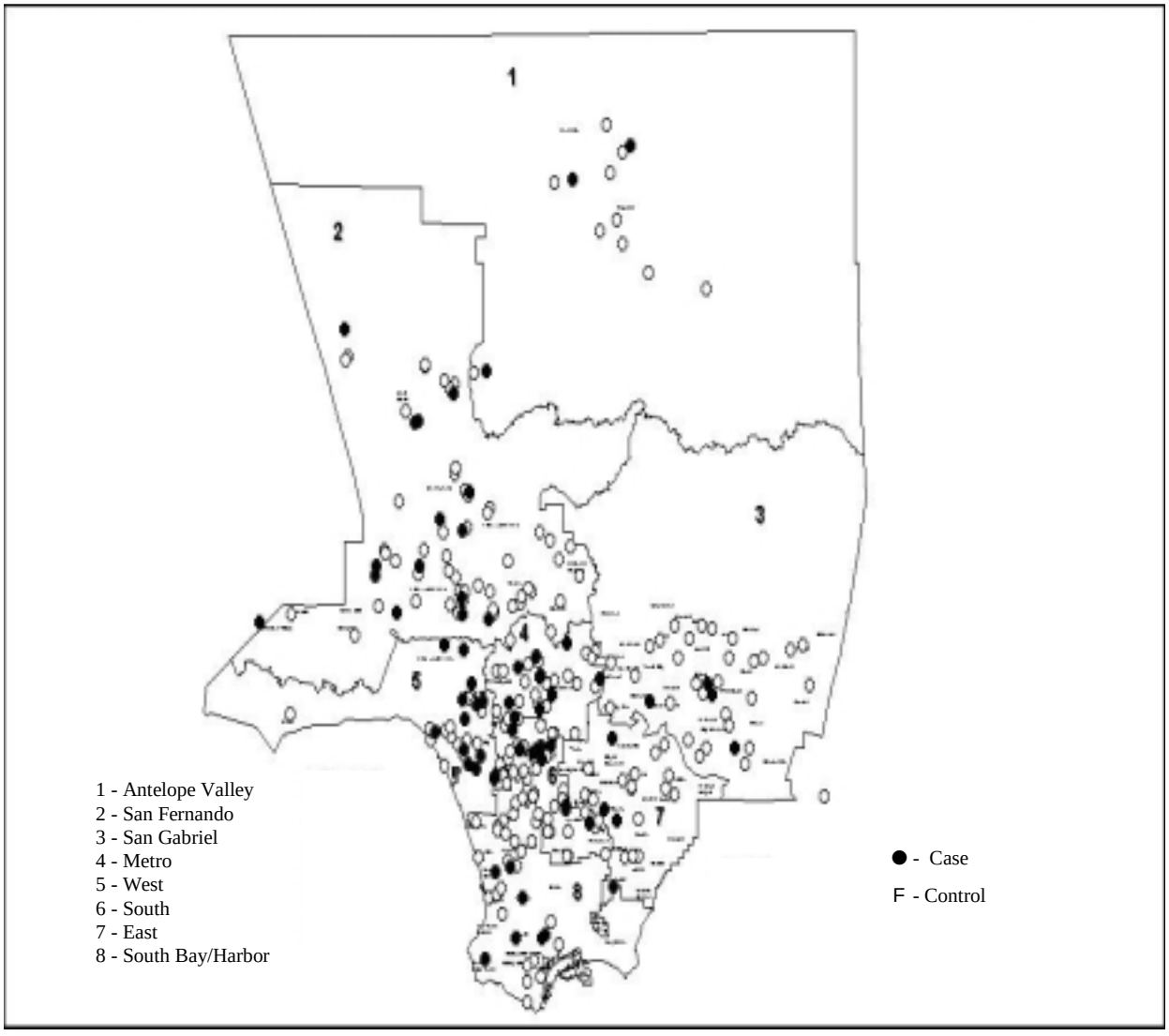
Characteristics			**%**
Race	African American		17
	Asian		3
	Hispanic		16
	White		53
	Other		10
	Unknown		1
Gender	Male		51
	Female		49
Age	< 5		14
	5 –14		1
	15 – 44		17
	45 – 64		21
	65 +		47
Mean Age (in years)			55 (s.d. 28)
Source of admission	Home		92
	Long-term Care Facility		5
	Acute Inpatient Hospital Care		3
Mean length of stay (in days)			9 (s.d. 7)
Expected source of payment for hospitalization			
Medicare			42
Medi-cal/County Indigent Program			22
HMO/PPO			30
Private insurance			3
Self-pay			2
Military			<1
Underlying medical conditions		Yes	74
		No	26
Outcome	Died		17
	Survived		83
Penicillin nonsusceptibility		Yes	25
		No	75

TABLE 2: Characteristics Associated with Having IPD Nonsusceptible to Penicillin (N = 283)

Characteristics		Nonsusceptible n	Nonsusceptible %	Susceptible n	Susceptible %	p-value*
Race	African American	14	20	33	16	.86
	Hispanic	10	14	35	17	
	White	38	54	110	53	
	Other	9	13	29	14	
Gender	Men	40	56	104	49	.36
	Women	32	44	107	51	
Age (in years)	< 18	15	21	27	13	.04
	18 – 64	19	26	88	42	
	65 +	38	53	96	46	
Source of admission (≥60 years, n=143)						.56**
	Long-term care facility	4	10	10	10	
	Home	35	90	94	90	
Length of stay (in days) Mean ± sd		9 ± 6		9 ± 7		.73***
Outcome	Died	11	15	37	18	.66
	Survived	61	85	174	82	
Underlying medical condition	Yes	52	72	157	74	.72
	No	20	28	54	26	

*Pearson's χ^2 used unless otherwise noted. **Fisher's Exact Test. ***Wilcoxon 2-Sample Test.

MAP 1. Map of place of residence for PNSP cases (black dots) and controls (white dots). The bold-faced numbers and boundaries represent service planning areas (SPAs) in Los Angeles County. Six percent (4) of the cases and 2% (4) of the controls could not be mapped.



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GROUP A STREPTOCOCCAL INVASIVE DISEASE

BACKGROUND

Group A Streptococcus (GAS), *Streptococcus pyogenes*, a common cause of pharyngitis and uncomplicated skin and soft tissue infections, can also cause serious invasive disease. In the late 1980s, reports of severe invasive GAS infections, including streptococcal toxic shock syndrome and necrotizing fasciitis, began to appear with increasing frequency worldwide. Various theories have been offered to explain the apparent increase and severity of streptococcal infections in recent years, including possible changes in virulence of circulating strains and changes in host susceptibility. GAS invasive disease is not a legislatively-mandated reportable disease in California. Following a cluster of severe invasive GAS infections in previously healthy children in Southern California in 1993, the Acute Communicable Disease Control Unit requested reporting of GAS invasive disease from laboratories, hospitals, and health-care providers in Los Angeles County.

METHODS

GAS invasive disease is defined as isolation of *Streptococcus pyogenes* from a normally sterile body site (blood, cerebrospinal fluid, pleural fluid, peritoneal fluid, bone, joint fluid, or from tissue collected during surgical procedures). GAS invasive disease includes three potentially overlapping clinical syndromes:

Streptococcal toxic shock syndrome (STSS) - characterized by early shock and multiorgan system failure;

Necrotizing fasciitis (NF) -necrosis of subcutaneous soft tissue and skin with signs of severe systemic disease;

Sterile site infections that do not meet the clinical criteria for STSS or NF, including nonfocal bacteremia, and focal infections (e.g., meningitis, pneumonia, peritonitis, osteomyelitis, septic arthritis, and deep soft tissue infections) with or without bacteremia.

Since reporting of GAS invasive disease was initiated in 1994, surveillance methods have varied from mainly passive during 1994 and most of 1995 to county-wide active surveillance between September 1995 and July 1996. Since July 1996, the Communicable Disease Active Surveillance Project (CDAS) has conducted stimulated passive surveillance for GAS invasive diseases, along with several other nonmandated reportable diseases of Public Health importance, in approximately 60% of laboratories and hospitals in LAC.

RESULTS

In 2000, 154 cases of GAS invasive disease were reported, for a crude incidence rate of 1.67 cases per 100,000 population. Thirty-one reports of skin/soft tissue infections were excluded because they did not meet the case definition for invasive disease. Of 61 cases for which outcome was known, there were 13 deaths, for an estimated case fatality rate of 21%. The frequencies of total GAS invasive disease, STSS and NF cases for years 1994-2000 are shown in Table 1.

Table 1. Frequency of Invasive GAS, STSS and NF
Los Angeles County, 1994-2000

Year	Invasive GAS	STSS		NF	
		N	(%)	N	(%)
1994	83	29	(35)	18	(22)
1995	103	16	(16)	17	(17)
1996	175	9	(5)	13	(7)
1997	205	7	(3)	9	(4)
1998	128	8	(6)	13	(10)
1999	114	6	(5)	11	(10)
2000	154	8	(5)	20	(13)

Focus of Infection: Approximately half (50%) of invasive GAS disease were bacteremia cases without other identified focuses of infection. (Table 2).

Table 2. Clinical Features Associated with Invasive GAS Disease Cases Los Angeles County, 2000 (N = 154)

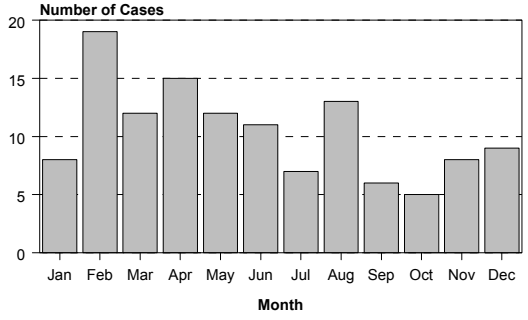
Focus of Infection	No. of patients* (%)	Age (yr) Median Range	Death No. (%)**
Skin-soft tissue infection			
Necrotizing fasciitis	20 (13)	54 (12-90)	4/13 (31)
Other	25 (16)	43 (0.6-88)	2/9 (22)
Toxic Shock Syndrome (TSS)	8 (5)	36 (4-68)	1/7 (14)
Pneumonia	12 (8)	44 (2-84)	0/8 (0)
Septic arthritis/osteomyelitis	14 (9)	40 (3-81)	0/6 (0)
Bacteremia (without septic focus)	77 (50)	56 (0.04-92)	6/21 (29)
Endocarditis	1(0.6)	22	0/0
Total	154	52 (0.04-92)	13/61 (21)

*Categories are not mutually exclusive. Two necrotizing fasciitis cases also had TSS and one septic arthritis also had TSS.
**Calculated only for those cases with available outcome data.

Seasonality: Cases occurred throughout the year but were more frequent during the winter and spring months (Figure 1). The pronounced winter/spring seasonality commonly associated with noninvasive GAS infections, however, was not observed.

Figure 1

GAS Invasive Disease
By Month of Specimen Collection
Los Angeles County, 2000



Age, Gender, Race/Ethnicity: The mean age of invasive GAS cases for which age data were available (n=153) was 48 years (median 52 years, range 7 days to 92 years). There were slightly more male cases (82) than female cases (71). Race/ethnicity data were available for 95 cases. Of these, 48 (51%) were non-Hispanic White, 37 (39%) were Hispanic, 7 (7%) were Asian, and 3 (3%) were Black.

Necrotizing Fasciitis: NF was reported in 20 (13%) cases; 14 (70%) of the cases were male. The mean age of NF cases was 54 years (median 54 years, range 12-90 years). Outcome was reported for 13 of the 20 NF cases with a case fatality rate of 31% (4/13). Two patients with NF were also diagnosed with streptococcal toxic shock syndrome.

COMMENTS

These data are subject to several limitations. First, changes in surveillance methods over the study period make meaningful year-to-year comparisons difficult. Completeness of invasive GAS reporting in LAC has not been assessed. The Center for Disease Control and Prevention estimates that the national incidence rate of invasive GAS disease is 1.5-3.5 cases per 100,000 population, compared to the LAC rate of 1.67 cases per 100,000 in 2000. Second, invasive GAS surveillance is mainly laboratory-based and detailed demographic and clinical data are rarely included with the initial report. Hospital record review of reported invasive GAS cases would have provided more complete data but was done for only a small number of cases. It is likely that the number of deaths and the occurrence of additional foci of infections in bacteremic cases are substantially underestimated.

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INVASIVE PNEUMOCOCCAL DISEASE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERNS FOR STREPTOCOCCUS PNEUMONIAE IN LOS ANGELES COUNTY, 2000

BACKGROUND

Streptococcus pneumoniae infection is the leading cause of pneumonia, bacteremia, and meningitis in the United States. Since 1995, the Los Angeles County (LAC) Department of Health Services (DHS) has operated a laboratory- and hospital-infection-control-based surveillance system for invasive pneumococcal disease (IPD). IPD was selected for surveillance to measure the incidence in LAC, track antibiotic resistance patterns, potentially monitor immunization efficacy, and target vaccine usage.

Table 1: MIC Breakpoints for Selected Agents Used to Treat *Streptococcus pneumoniae* Infection

Antimicrobial	MIC (μg/mL) Susceptible	Intermediate	Resistant
Penicillin	≤0.06	0.12-1.0	≥2.0
3rd generation Cephalosporin (cefotaxime,ceftriaxone,cefuroxime)	≤0.5	1.0	≥2.0
Erythromycin	≤0.25	0.5	≥1.0
Trimethoprim-sulfamethoxazole (TMP-S)	≤0.5/9.5	1/19-2/38	≥4/76

A major development for IPD in 2000 was the Food and Drug Administration's approval of a conjugate vaccine protecting children less than two years of age. Previously, the only available vaccine, polysaccharide vaccine, could not protect this high-risk age group. Studies have indicated that the vaccine is safe and effective (1).

Table 2: Characteristics of IPD Cases Los Angeles County, 1997-2000

Characteristics*	1997 (N=818)	1998 (N=814)	1999 (N=894)	2000 (N=760)
Male:Female Ratio	1.10:1.00	1.06:1.00	1.03:1.00	1.01:1.00
Age (years)				
Mean	44	44	47	43
Median	49	50	53	48
Range	1 mo.-106	<1 day–102	1 day–100	<1 day –101
Case fatality rate	15% (59/383)	15% (53/346)	17% (55/328)	13% (42/320)
Culture site				
Blood only	771 (95%)	776 (96%)	836 (94%)	703 (93%)
CSF/CSF&Blood	30 (4%)	28 (3%)	44 (5%)	33 (4%)
Other	13 (2%)	10 (1%)	14 (2%)	24 (3%)

*Data not available on race/ethnicity and characteristic information not available for all cases.

Increasing antimicrobial resistance continues to be a problem with pneumococcal disease. In a report by the Centers for Disease Control and Prevention Working Group on *S. pneumoniae*, their nationwide population-based surveillance system observed a percent increase of penicillin nonsusceptible *S. pneumoniae* isolates from 14% in 1993-1994 to 27% in 1999 (2,3). Other classes of antimicrobials such as the macrolides, cephalosporins, and fluoroquinolones also have developed resistance.

The following is a description of the 2000 incidence of reported IPD and *S. pneumoniae* antimicrobial susceptibility patterns in individuals residing in LAC (excluding the cities of Long Beach and Pasadena).

METHODS

Cases were defined as LAC residents with a positive isolate for *S. pneumoniae* from a normally sterile site collected in 2000. To calculate incidence rates, population data were derived from the 1990 census using sophisticated estimation techniques developed by the LAC Urban Research Section. Antimicrobial susceptibility was determined by disk diffusion or dilution diffusion. It was assumed that minimum inhibitory concentration (MIC) breakpoints utilized by participating laboratories were based on the National Committee for Clinical Laboratory Standards. The breakpoints for selected antimicrobial agents are illustrated in Table 1. An isolate of *S. pneumoniae* was considered nonsusceptible to an antimicrobial agent if the results indicated intermediate or high-level resistance. Data were entered in Microsoft Access 97 and analyzed using Epi-Info 6.04 and SAS Version 6.12.

DATA ANALYSIS

The annual incidence of reported IPD decreased 16% from 9.8 cases per 100,000 (n=894) in 1999 to 8.2 cases in 2000 (n=760). As indicated by Table 2, the male-to-female rate ratios indicated that there were slightly more males who acquired IPD. In 2000, the mean age for IPD cases was 43 years (median 48 years, range <1 day to 101 years), which was comparable to the previous three years.

In 2000, the case-fatality rate was 13%, which was the lowest rate in four years (Table 2). The validity of this data is questionable since outcome status of 58% of the cases for 2000 were reported as "unknown," although it should be noted that the percent "unknown" stayed constant for the previous three years. The case-fatality rate may be underestimated since reporting of positive isolates is required within 24 hours and many times the final outcome of current infection has not yet been determined. The distribution of cases by culture site varied little from 1997 to 2000. As in previous years, mortality in 2000 was not significantly associated with having

Figure 1: Incidence Rates of IPD Cases by Age, Los Angeles County, 1997-2000

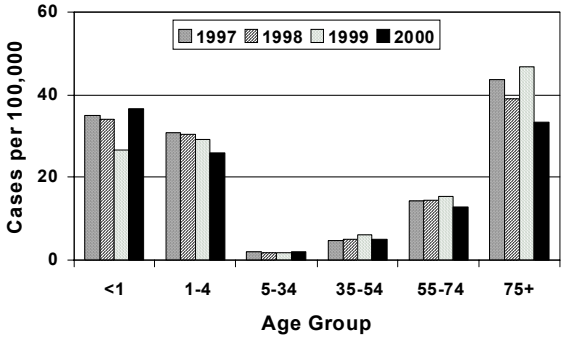
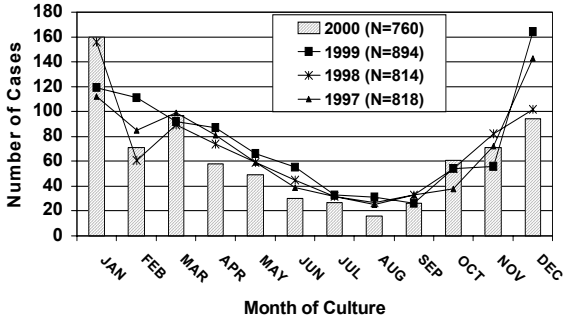


Figure 2: IPD Cases By Month of Culture Los Angeles County, 1997-2000



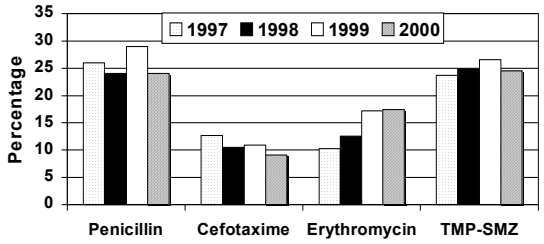
meningitis (odds ratio [OR]: 1.11; 95% confidence interval: 0.19 to 4.38, p=0.55).

For 2000, the highest age-specific incidence rates occurred in children under five years and adults 75 years and over, which is common with IPD (Figure 1). Comparing 2000 to 1999, the age-specific incidence rates decreased in all age groups except in infants less-than-one-year (+38%).

The IPD cases for 1997-2000 followed the typical seasonal pattern, peaking in late winter, then gradually declining through spring. The pattern observed by month for 2000 was very similar to what was seen in 1997 (Figure 2).

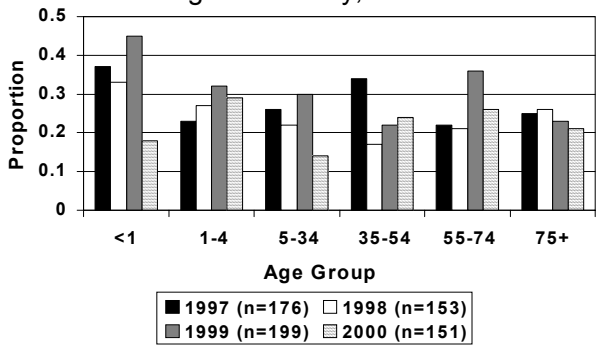
In 2000, Inglewood District had the highest crude rate of IPD at 13.1 per 100,000 population (54 cases) followed by Glendale with a rate of 11.5 (39) and West Valley with 10.8 (79). The West Valley District had the highest number of cases. Inglewood District continued to have the highest rate (13.4 cases per 100,000) even after adjusting for age (using the age groups in Figure 1). From 1998-2000, Southwest District was among the top three districts with the highest age-adjusted rates.

Figure 3: IPD Cases Nonsusceptible to Selected Antimicrobial Agents
Los Angeles County, 1997-2000



From 1997 to 2000, the proportion of penicillin nonsusceptible *Streptococcus pneumoniae* (PNSP) isolates has fluctuated from a low of 24% in 1998 and 2000 to a high of 29% in 1999 (Figure 3). The fluctuation of PNSP by year was not significant (χ^2=7.12, p-value=0.07). The percent of cases nonsusceptible to erythromycin increased from 1997 to 2000 and cefotaxime decreased while trimethoprim-sulfamethoxazole (TMP-SMZ) remained about the same.

Figure 4: PNSP Cases by Age
Los Angeles County, 1997-2000



In 2000, the proportion of PNSP cases was lower than the previous year among all age groups except adults 35-54 years. The largest decrease (-60%) of penicillin resistance from 1999 to 2000 was in infants less than one year (Figure 4). In 2000, there was not a significant difference between age groups

and penicillin nonsusceptibility (χ^2=7.28, p-value=0.20). Also mortality was not significantly associated with penicillin nonsusceptibility.

DISCUSSION

The DHS observed a decrease in incidence and antibiotic nonsusceptibility for cases of IPD in 2000. The very young and the elderly had a higher risk of acquiring IPD. Resistance was not associated with increased mortality. For more information regarding antimicrobial resistance and IPD in LAC, see the other 2000 special studies report on "Factors Associated with Acquiring Penicillin Nonsusceptible Invasive Pneumococcal Disease in Los Angeles County."

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LOS ANGELES COUNTY INFLUENZA SURVEILLANCE 2000-2001: WHO KNEW WHAT FLU WOULD DO?

Because of difficulties producing the 2000-2001 influenza vaccine, distribution was postponed and forecasts assumed this would result in an especially severe season. However, despite the vaccine delay and subsequent shortages, the influenza season in Los Angeles County (LAC) was actually quite mild; the onset of influenza activity occurred several weeks later than usual, the peak in activity was far less pronounced than the previous season, and overall, the incidence and impact of influenza was substantially less extreme than expected. Similarly, during the 2000-2001 season, there were no confirmed influenza outbreaks in LAC (compared to five confirmed outbreaks during 1999-2000), and nationally, the influenza/pneumococcal mortality rate seldom exceeded the seasonal baseline or the epidemic threshold.

The following summarizes the major events which occurred during the 2000-2001 influenza season as well as the surveillance efforts which detail the season's occurrence and impact of influenza.

CHRONOLOGICAL EVENT SUMMARY

During the 2000-2001 season, there were many events that potentially influenced the onset, acceleration and duration of influenza (Table 1). First and foremost was the vaccine delay; because of difficulties in developing the vaccine needed for the 2000-2001 season, vaccine distribution did not begin in LAC until November 1, 2000, more than a month later than ususal and three weeks after the first confirmed influenza case of the season was reported. Moreover, since only about 60% of the LAC Department of Health Service's annual allocation of vaccine was received from the State, supplies quickly ran out. Vaccination was able to resume on November 26, 2000.

Despite the vaccine delay and initial shortage, the overall incidence of influenza remained low. In addition, despite the slow start to the 2000-2001 season, the peak in activity still occurred at the usual time for LAC, just prior to the new year.

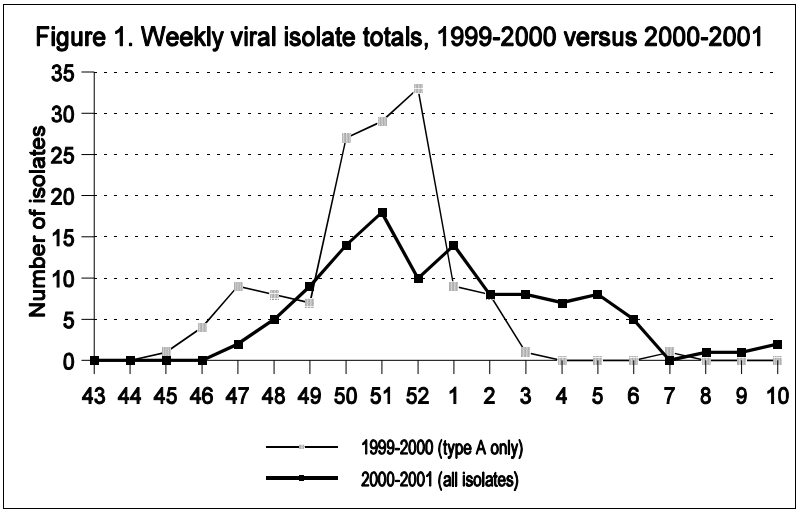
VIRAL ISOLATE COLLECTION

In order to assess the seasonal pattern of influenza activity in LAC, during the winter months, influenza viral isolates are reported weekly to ACDC from Kaiser Permanente and Cedars Sinai laboratories. When combined with clinical information from the community, these isolate reports are a valuable resource since they effectively describe the onset, peak and duration of influenza activity. In addition, since this surveillance method is fairly consistent from season to season, it provides a practical means of comparing seasons.

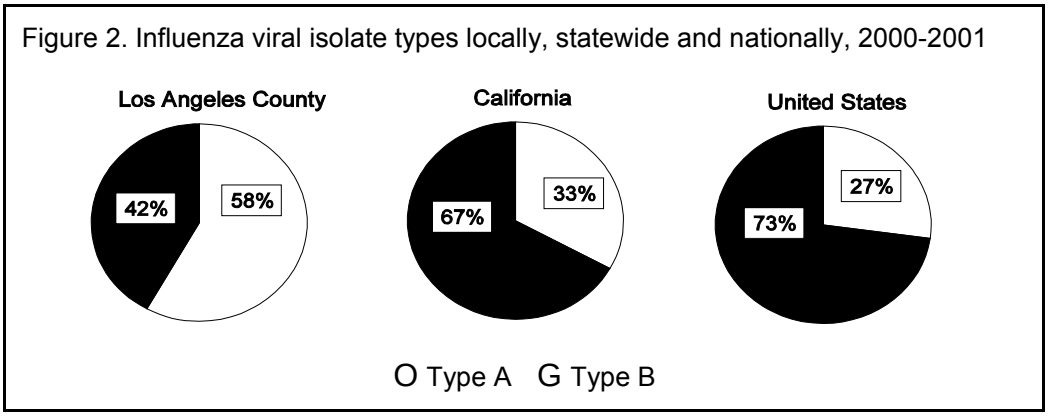
Table 1. Chronological Event Summary for Influenza Season 2000-2001

Week	Dates	Events
38	9/17 - 9/23	**Vaccine is delayed**. In typical years, influenza vaccine distribution begins in late September to early October. However, because of difficulties in cultivating the viruses needed to create the 2000-2001 vaccine, distribution was postponed. The potential consequences of the delay were unknown; the FDA warned of potential vaccine shortages, whereas the CDC predicted delay but no shortage.
41	10/8 - 10/14	**First confirmed case in L.A. County (10/11).** The first recognized case of influenza (type B) is reported from Kaiser Permanente laboratory.
44	10/29 - 11/4	**Vaccine distribution begins (11/1). Supply and demand in action.** Community vaccine programs were deluged by people hoping to be vaccinated, most likely a consequence of the increased publicity surrounding this year's vaccine distribution. Only about 60% of the Department of Health Service's annual allocation of vaccine was received from the State. Presumably, the private sector experience was similar.
45	11/5 - 11/11	**Vaccine runs out.** Beginning with Service Planning Areas 1, 2, 3, and 7, vaccine supplies were exhausted and clinic sessions were canceled until the remaining supply was received.
47	11/19 - 11/25	**Anitviral medication as prophylaxis.** On 11/20, the FDA approves the use of Tamiflu (oseltamivir) to prevent influenza among those unable to be vaccinated.
48	11/26 - 12/2	**Vaccination resumes. Incidence of influenza remains low.** The remaining publically administered vaccine is delivered to clinics and administration resumes. Fortunately, the number of confirmed influenza cases remained low with only 4 official isolates reported as of 11/30. The number of isolates was substantially lower than the previous year, which had a cumulative total of 24 isolates by the same date.
50 - 51	12/10 - 12/23	**Typical peak of influenza season.** Even though the 2000-2001 season began later than expected, the peak in activity occurred as usual, just prior to the new year.
8 - 10	2/18 - 3/10	**Typical end of influenza season.** Influenza activity tapered longer into the new year than the previous season, but still culminated as expected.

Figure 1 shows the weekly total number of isolates reported from the 2000-2001 season compared to the 1999-2000 season. Overall, there was a 20% decrease in the total number of influenza isolates reported during 2000-2001 compared to the previous season. In addition, while activity peaked roughly around the same time during the last two seasons, during 2000-2001, the peak was considerably less pronounced and activity extend longer into the new year.



Another differentiating feature of the 2000-2001 season was the high proportion of type B influenza activity nationally and *especially* locally (Figure 2). During the 1999-2000 season, only one isolate of type B influenza was reported in LAC, whereas during the 2000-2001 season, more than half (58%) of the influenza isolates were type B. Across California, roughly a third of the isolates reported during 2000-2001 were type B, and nationally, slightly more than a fourth were type B.



INVASIVE PNEUMOCOCCAL DISEASE

Invasive pneumococcal disease (IPD) can also approximate the intensity and impact of influenza; IPD is often a consequence of severe influenza infection and, as such, seasonal IPD rates typically

match the seasonal pattern of influenza rates. As shown in figures 3 and 4, the weekly total of IPD cases mirror the weekly total of reported influenza viral isolates. During 1999-2000, both diseases

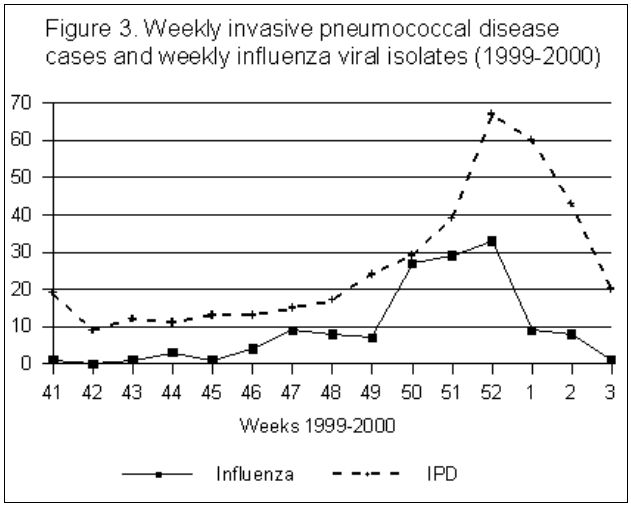


Figure 3. Weekly invasive pneumococcal disease cases and weekly influenza viral isolates (1999-2000)

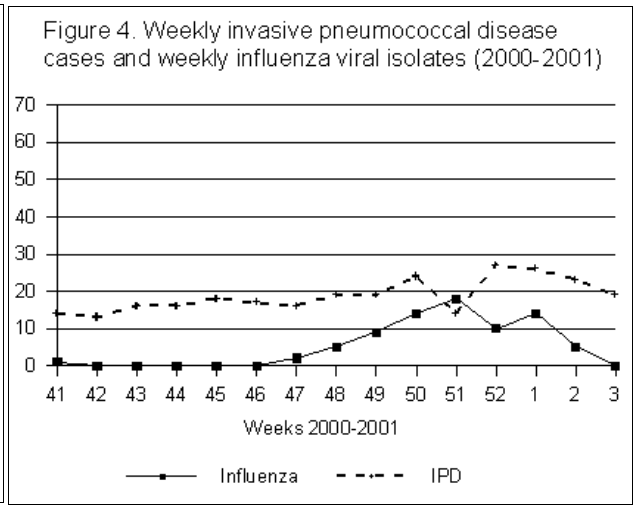


Figure 4. Weekly invasive pneumococcal disease cases and weekly influenza viral isolates (2000-2001)

show a sharp peak in incidence around the new year, whereas during 2000-2001, the incidence for both is relatively flat, a finding which is consistent with the mild influenza season.

INFLUENZA/PNEUMONIA MORTALITY

Every week as a part of the 122 Cities Mortality Reporting Program, the LAC Department of Health Services reports to the CDC the number of pneumonia and influenza deaths which occur in the largest cities in LAC (Los Angeles, Glendale, Pasadena, and Long Beach). In 1999, to correct an underreporting of pneumonia deaths, the case definition was expanded from deaths due to pneumonia listed as the *primary* cause of death to deaths from pneumonia listed *anywhere* on the death certificate. However, this modification has not been incorporated into the LAC system due to technical difficulties. In addition, the LAC mortality information is reported by its file date, which may deviate from the actual date of occurrence.

The mild influenza season was reflected by the stable influenza/pneumonia mortality rate. As shown in graph 5, while the number of influenza/pneumonia deaths in LAC fluctuated from week to week, during the height of influenza season, the proportion of deaths in LAC (where pneumonia is classified as the primary cause) remained relatively flat and never exceeded 10% of all deaths.

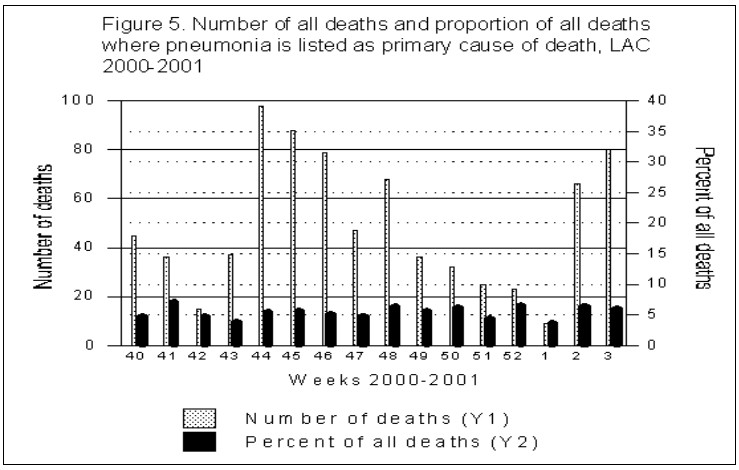
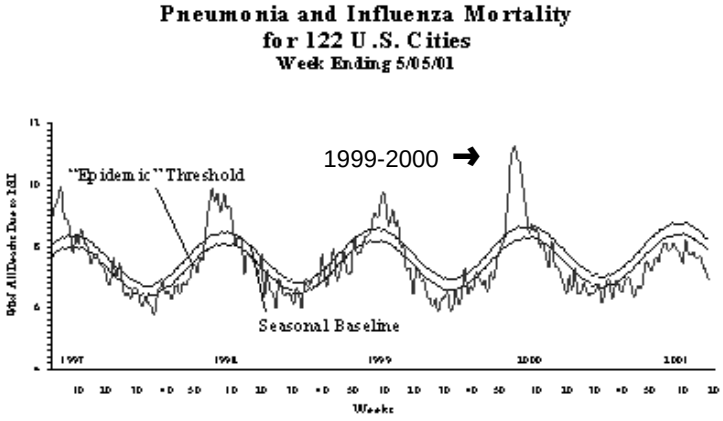


Figure 6. Pneumonia and influenza mortality for 122 Cities, CDC, Week ending 5/05/01



The national mortality findings were similar. Consistent with other surveillance findings which have indicated that this has been a mild influenza season, the number of pneumonia and influenza deaths have been low compared to historical averages (Figure 6). While last season (1999 - 2000) there was a dramatic peak in pneumonia and influenza mortality, this season, the number of pneumonia and influenza deaths reported never exceeded the seasonal baseline, much less the

epidemic threshold. These findings as well as additional influenza-related information is available at http://www.cdc.gov/ncidod/diseases/flu/fluvirus.htm.

CONCLUSION

Overall, the 2000-2001 season provides an interesting model for the effectiveness of surveillance methods during a mild influenza season. Findings provided by more direct methods of surveillance, such as the weekly viral isolate reports, continued to reflect the seasonal pattern of influenza activity (i.e., its onset, peak and duration), albeit to a lesser extent than more intense years. In contrast, findings from indirect methods, such as invasive pneumococcal disease and mortality rates, which rely upon the secondary consequences of influenza, were similar to rates which occur outside of influenza season. Thus, while indirect methods validated the low intensity of the season, if taken out of context, they cannot detect the presence of influenza activity. Future efforts should concentrate on expanding methods which can effectively characterize the influenza season during both severe and mild seasons.

OUTBREAK OF "NORWALK-LIKE VIRUS" GASTROENTERITIS ASSOCIATED WITH FOODHANDLERS: EVIDENCE OF PROLONGED VIRAL SHEDDING USING NEW DNA PRIMERS

"Norwalk-like viruses" (NLV) are the most common cause of foodborne illness in the United States accounting for an estimated 23 million cases of foodborne illness each year.[1] Symptoms of NLV infection start within 2 days after exposure and include nausea, vomiting and diarrhea that usually last 24- 48 hours.[2] The most common modes of transmission are contamination of food and water by feces and person-to-person transmission. Airborne spread via aerosolized vomitus also has been reported.[3,4]

Foodhandlers are often associated with NLV transmission. Transmission has been documented from foodhandlers both before and after they resolve symptoms of NLV infection.[5-8] Recommendations differ on how to prevent the transmission of NLV by foodhandlers. In 1990, the Centers for Disease Control and Prevention (CDC) recommended restricting foodhandlers from preparing food for at least 2 days after resolution of gastrointestinal illness.[9] However in 2001, the CDC issued new guidelines which stated that foodhandlers should maintain strict personal hygiene at all times but did not specify for how long foodhandlers should be removed from work.[10] The 1999 Food Code issued by the Food and Drug Administration recommends restricting foodhandlers from preparing food only while symptomatic with vomiting or diarrhea.[11] The National Restaurant Association and many state departments of health use this code as a model.

Experimental volunteer studies have documented Norwalk virus (the prototype NLV) shedding in stool by electron microscopy (up to 5 days),[12] reverse transcriptase-polymerase chain reaction (RT-PCR) (6 days),[13] and enzyme-linked immunoassays (13 days)[14] after exposure to Norwalk virus; maximal shedding occurs in the first 48 to 72 hours. Duration of shedding after resolution of gastrointestinal symptoms has not been systematically documented; this has important implications for how long to remove foodhandlers from preparing food. Based on the results of an investigation of a restaurant-associated outbreak of NLV, we were able to address this question.

Between March 27 and 31, 2000, the Acute Communicable Disease Control (ACDC) Unit received reports of 19 people, from 5 different groups, who became ill after eating at a restaurant in Los Angeles County (LAC). Interviews with 10 of the 19 restaurant patrons revealed that they had nausea, vomiting, or diarrhea within 24 to 48 hours after eating at this restaurant on either March 25 or 26. Based on these symptoms NLV was suspected. On March 31, during a restaurant inspection prompted by these reports, the environmental health investigator learned of 17 employees who also had gastrointestinal symptoms. Given the high risk of NLV transmission by foodhandlers, the restaurant was shut down and all employees had to be cleared by the health department before returning to work (i.e., they had to be free of gastrointestinal symptoms for at least 2 days).

ACDC investigated this outbreak to confirm the etiology of the outbreak and to determine the incidence of gastroenteritis among the employees during the last 2 weeks of March 2000. Results from this investigation allowed us to calculate the length of NLV shedding in stool after resolution of gastrointestinal symptoms.

METHODS

During April 1 to 4, employees of the restaurant were interviewed about symptoms of gastroenteritis for the last 2 weeks of March 2000. Questions included the type of symptoms, the date of onset, the duration of symptoms, and whether or not the employee worked while ill. In this outbreak, a case of acute gastroenteritis was defined to be 3 or more loose stools in 24 hours or vomiting. A possible case of gastroenteritis was 1 or 2 loose stools in 24 hours or nausea with either chills or fever.

The laboratory investigation consisted of collecting single stool samples from restaurant employees and patrons. The samples were tested for the presence of NLV using Region B RT-PCR primers at the Los Angeles County Public Health Laboratory. Selected positive RT-PCR amplicons were sequenced at an outside laboratory. The number of days shedding NLV after resolution of symptoms was calculated by subtracting the date of last gastrointestinal symptoms from the date of stool collection for positive specimens.

Epi-Info 6.04c (Centers for Disease Control and Prevention, Atlanta, GA, 1999) was used for data management and analysis.

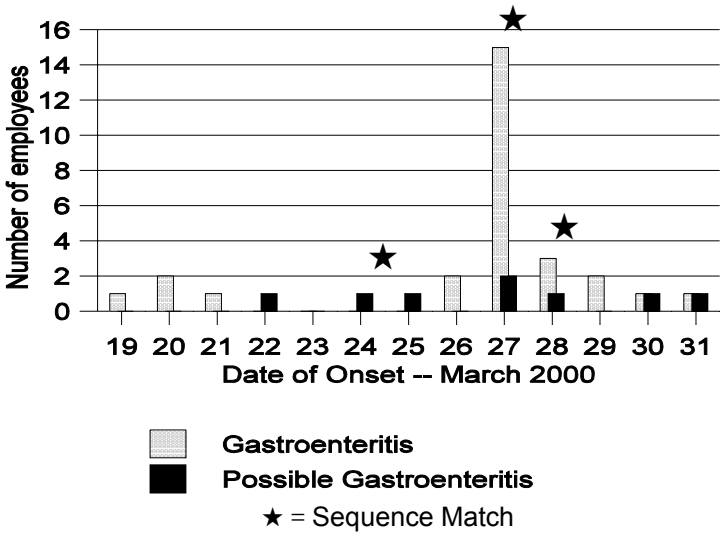
RESULTS

All 71 employees of Restaurant A were interviewed; 28 (39%) met the case definition of acute gastroenteritis and 7 (10%) were possible case-patients; the remaining 36 (51%) employees were asymptomatic. Figure 1 displays the epidemiologic curve of this outbreak. Half of the employees for whom information was available (16 of 32 employees) admitted to working while ill.

Laboratory investigation revealed that 12 (57%) of 21 employees who met the case definition for acute gastroenteritis and who submitted stool samples tested positive for NLV. In contrast, only 1 (14%) of 7 possible case-patients tested positive for NLV and 4 (20%) of 20 asymptomatic employees who submitted stool samples also tested positive for NLV. Three samples (from a cook, a waitress, and a patron with symptom onset dates 3/24, 3/27, and 3/28, respectively) were submitted for DNA sequencing and all 3 were identical. Though only 2 of 8 case-patients had NLV in their stool 0 to 2 days after resolution of symptoms, 10 (77%) of 13 continued to shed NLV in their stool 3-11 days after resolution of gastrointestinal symptoms; one case-patient was still shedding at 11 days.

DISCUSSION

Figure1. Cases of Gastroenteritis and Possible Gastroenteritis Among Employees and One Patron by Onset Date of Illness (n=36)



NLV was suspected as the cause of this outbreak among restaurant employees and patrons based on clinical symptoms; this was confirmed by the laboratory results. The epidemiologic curve (Figure 1) shows that NLV may have been transmitted at a low level among restaurant employees for almost a week before the larger outbreak among restaurant employees and patrons. Patrons were exposed March 25-26 and the majority of employees were probably exposed at that time since most of the ill employees became ill between March 26-28, the same time as the restaurant patrons. We were unable to identify a single food item as the vehicle of transmission for the outbreak (data not shown). A cook who was ill with mild gastrointestinal symptoms for only one day on March 24 worked on March 25 and 26. Since the NLV in his stool was genetically identical to the virus in the stool of a patron who ate at the restaurant on March 26, the cook could have been the source of the large outbreak. However, more than one foodhandler may have been shedding and transmitting NLV during the weekend of March 25 to 26 leading to contamination of multiple food items.

Using the Region B RT-PCR primers, we found that the majority (77%) of foodhandlers shed NLV more than 3 days after resolution of gastrointestinal symptoms, with a maximum duration of shedding tested at 11 days after resolution of symptoms. What was unusual was that only 2 of 8 stools tested positive for NLV within 2 days after resolution of symptoms. Previous experimental studies have documented the highest rate of shedding in the first two days after exposure to virus. However, those studies used actual Norwalk virus while the agent in our outbreak was a Norwalk-like virus; it is possible that there are clinical differences in how quickly humans stop shedding different NLV strains.

Since stool samples were taken at only one point in time our estimates of the duration of shedding must be regarded as minimums since employees may have continued to shed NLV after we

collected their stool sample. Furthermore, the number of employees infected with NLV is probably underestimated since some may have stopped shedding NLV in their stool before the samples were collected.

Current recommendations from the CDC suggest to preferentially collect stool specimens within the first 48-72 hours after patients become ill, and from patients with watery or unformed stool.[10] However, we found that persons who had vomiting but no diarrhea (data not shown) were as likely to have a positive stool result as persons who had diarrhea. Our study indicates that the Region B RT-PCR primers may be sensitive enough to detect NLV in stool for up to 11 days after resolution of symptoms and from case-patients who have vomiting but not diarrhea. These findings should encourage the collection of stool samples longer than previously thought and from a wider variety of patients. Working with a local public health laboratory is essential to identify NLV. Tests for NLV are not commonly available in commercial laboratories.

To decide how long foodhandlers should be restricted from preparing food, better studies are needed to assess the risk of shedding NLV and transmission of the virus. These studies should include epidemiologic findings documenting both post-symptomatic and asymptomatic transmission of NLV by foodhandlers. RT-PCR is a sensitive and powerful tool, though in real world applications, it is assumed that at least 100-10,000 viral particles/ml of stool are required for a positive test.[10] However, since the estimated infective dose of NLV is only 10-100 particles, a positive test result suggests that there are sufficient viral particles for transmission of the disease if a foodhandler has poor hygiene. RT-PCR tests need to be developed that quantify the decrease in the viral load shedding after resolution of symptoms to quantify transmission risk. Region B RT-PCR primers only tests for the presence of NLV RNA; it still needs to be shown that the RNA is infectious, i.e., in an intact, infectious virion.

Given that half of the employees surveyed admitted to working while ill, we recommend enforcing the FDA Food Code Guidelines to restrict foodhandlers from working while symptomatic. We also suggest expanding the FDA recommendations to restrict foodhandlers for at least 2 days after gastrointestinal symptoms resolve according to the 1990 CDC recommendations. If the foodhandler no longer has diarrhea and adheres to adequate handwashing and gloving, as called for in the FDA Food Code, then there may be no need to restrict the foodhandler from work for longer than 48 hours even if they are still shedding NLV.

Finally, paid sick leave, which may not be commonly offered to hourly employees in the restaurant industry, may reduce the number of employees who work while ill and may have avoided this outbreak.

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PEDIATRIC HIV DISEASE
PEDIATRIC SPECTRUM OF DISEASE (PSD)

In March 1988, the Los Angeles County (LAC) Department of Health Services began conducting active surveillance for children HIV-exposed and infected under the age of 13 years as part of the Centers for Disease Control's national PSD research project. Case ascertainment included all children who had died with an AIDS or HIV diagnosis and all who were still alive and in medical care. As of December 31, 2000, with active case surveillance at the 10 major LAC pediatric referral centers, a total of 1,627 HIV exposed and infected children had been reported to PSD. This number includes 1,422 LAC resident children and 205 nonresident children receiving care in LAC (including those who had died). PSD collects information at baseline, when the child is initially evaluated for HIV and then every 6 months for the life of the child. Children who reach adolescence are followed until they are transferred to an adult AIDS clinic. Excluding those who have died or are lost to follow-up, 297 HIV-infected children and adolescents and 46 children of indeterminate status are under HIV care in LAC.

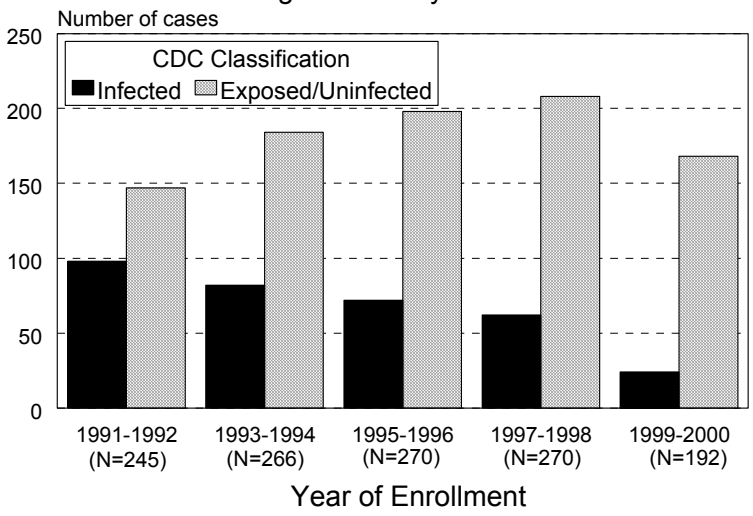
CDC CLASSIFICATION

Of the total 1,627 children reported to PSD through December 31, 2000, 593 were HIV-infected, 936 were perinatally exposed but uninfected, and 98 were exposed and of indeterminate HIV status due to the persistence of maternal HIV antibody. Of the 593 HIV-infected children, 309 or 52% had an AIDS-defining condition and met the CDC classification criteria for AIDS. Of these, 25 were diagnosed with an AIDS defining illness after 12 years of age. An additional 24 infected children 13 years or older met the adult AIDS definition with a CD4 lymphocyte count <400µL. In 2000, 80 HIV-exposed or infected children were reported to PSD of whom 6% had an AIDS diagnosis at last medical contact, an additional 10% were infected but without AIDS, 44% were of indeterminate status, and 40% were uninfected. Of the 13 infected children reported in 2000, 11 were identified after birth and 10 after 2 years of age. Four were non-LAC residents at the time of their HIV diagnosis. The proportion of infected children has decreased from 40% of the total children reported in 1991-1992 to 13% in 1999-2000 (Figure 1).

MODE OF TRANSMISSION

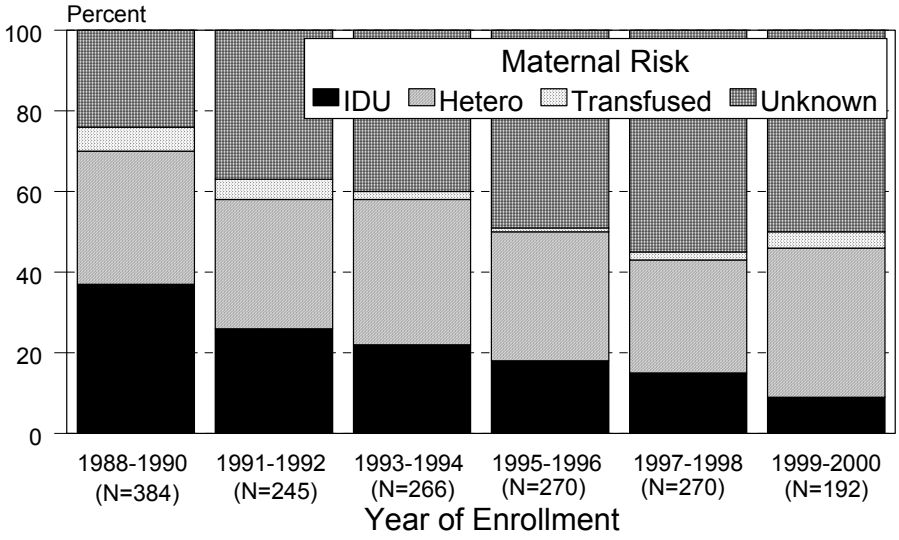
Among the 691 HIV-infected children and adolescents, including 98 children with indeterminate HIV status, 515 (75%) had perinatally acquired (PA) infection from an HIV-infected mother, 125 children (18%) were infected from a contaminated blood transfusion, and 39 (6%) were children with hemophilia or a coagulation disorder, and 12(1%) other or unknown transmission including two children who were infected due to breast feeding. Among the PA group, 22% had a mother who was an intravenous drug user (IDU), 11% had a mother who had sex with an IDU, 25% had a mother who had sex with an HIV+ or high-risk male, 4% had a mother infected through a blood transfusion, and 37% had a mother whose risk factor for HIV infection could not be identified. Sexual abuse is suspected as a risk factor for 4 children and confirmed for 1 child.

Figure 1: CDC Classification and Year of Child's Enrollment
Los Angeles County 1/91-12/00



Source: DHS, Pediatric Spectrum of HIV Disease Study

Figure 2. Maternal HIV Risk of Children with Perinatally Acquired HIV Exposure by Year of Child's Enrollment
Los Angeles County, 3/98 - 12/00



Source: DHS, Pediatric Spectrum of HIV Disease Study

The proportion of perinatally exposed children whose mother's risk factor for HIV was IDU has decreased from 37% in 1988-90 to 9% in 2000 (Figure 2). Correspondingly, the number of children infected due to an HIV-infected mother with unknown risk has increased each year from 24% in 1988-90, to 50% in 1999-2000.

DEMOGRAPHICS

Among the 691 HIV-infected and indeterminate children and adolescents reported, 34% were Black, 42% Hispanic, 20% White, 3% Asian, and 1% other/unknown. Of the 80 HIV-exposed and infected children reported in 2000, 38% were Black, 53% Hispanic, 7% White, and 2% other/unknown.

The distribution of HIV-infected and indeterminate children by gender shows slightly more males than females (52% vs. 48%), due to the disproportionate number of transfusion-associated and hemophiliac cases among males.

Most children (73%) had a biologic parent as their primary caretaker at the latest medical contact: 20% lived with another relative or were in foster care, 3% with adoptive parents, and 5% in other or unknown living arrangements. The PA group was more likely to be living in foster care or with another relative than the transfused and hemophiliacs (23% vs. 5%, and 3% respectively). Within the PA group, the Hispanics were the least likely to be in foster care or living with another relative (14% vs. 32% for Blacks and 30% for Whites).

CASE FATALITY AND SURVIVAL

The cumulative fatality rate for AIDS cases was 64% (198/309). Fourteen or 4% of the children not meeting the AIDS case definition have died. The mean age at AIDS diagnosis for the PA cases was 29 months (median 14.0 months) compared to the mean age at AIDS diagnosis of 89 months for the transfused cases (median 89 months), and 160 months for the hemophiliacs (median 143 months).

Among the 343 HIV-infected and indeterminate children still alive and followed by PSD, 16% were less than 2 years of age, 31% were between 2-7 years, 27% were 8-12 years, and 26% were 13 years or greater.

PRENATAL ZDV AND PERINATAL TRANSMISSION

Beginning in 1994, zidovudine (ZDV) use during pregnancy, labor, and delivery became a recognized means to prevent perinatal HIV transmission. Of the 611 infants born in 1995-2000 to HIV-infected women and reported to PSD, 449 (73%) of their mothers received ZDV during pregnancy; 492(81%) received prenatal care. Similarly, 451 (74%) received ZDV during labor and delivery. In 2000, 93% received prenatal care, 89% received antiretrovirals either during pregnancy

or labor and delivery, and 73% of the mothers received both. Compared to the 20-25% transmission rate observed before 1994, the overall rate of transmission for all children born in 1995-00 and reported to PSD was 10%. The C-section rate in LAC among children reported to PSD has increased from 20-30% before 1999 to 51% in 2000.

UNIVERSAL OFFERING OF PRENATAL HIV TESTING AND COUNSELING

As of January 1, 1996, all prenatal providers are legally required to offer HIV testing and counseling and document the offering in the patient's medical record. Statistics from six health centers who report directly to Acute Communicable Disease Control (ACDC) showed a 75% acceptance rate for 2000. Three HIV-positive women were identified in 2000. ACDC continues to evaluate risk assessment data on pregnant women who test HIV positive. Eighty-two women since 1989 have been identified in LAC clinics; 58 (71%) reported risk assessment information to ACDC. Thirty (52%) of these women could not identify any known risk factor for HIV infection. Women identified as HIV positive are referred to tertiary care centers to receive specialized care for themselves and their unborn infants.

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REPTILE-ASSOCIATED SALMONELLOSIS - A CONTINUING PROBLEM

In early September 2000, Los Angeles County (LAC) Acute Communicable Disease Control (ACDC) was contacted by two different public health nurses (PHNs) working in the same health center regarding two cases of *Salmonella* group B in unrelated children. The epidemiological investigation revealed that both families had purchased small red-eared slider turtles at the same local swap meet in the month before their children became ill. The serotype for both cases was later determined to be *Salmonella* ser. San Diego, an uncommon serotype. ACDC receives periodic complaints about the illegal sale of small turtles at swap meets. The two *S*. San Diego cases, as well as other salmonellosis cases linked to pet turtles, prompted a press release concerning health risks associated with turtles.

The US banned the interstate commercial distribution of pet turtles <4 inches long in 1975 because it was estimated that turtle exposure caused 14% of all salmonellosis cases in the US at that time. In California, regulations prohibiting the sale of turtles <4 inches long (*California Code of Regulation*, Title 17, Section 2612.1) have been in effect since 1972. Enforcement of this ban has been difficult. Turtles and other reptiles have remained popular pets in the US; their popularity appears to increase after movie and televison specials about dinosaurs and reptiles.

Long known to carry *Salmonella* bacteria, reptiles continue be a source of salmonellosis infection in humans who have contact with them. Epidemiological investigations of 990 reported salmonellosis cases in LAC in 2000 revealed that 10% (95 cases) had exposure to reptiles during their incubation period. Turtle exposure was identified in 5% (46 cases), iguana exposure in 2% (16 cases), snake exposure in 2% (20 cases), and other lizard exposure in 1% (13 cases). Of the 95 cases having reptile exposure, 20% (19 cases) were hospitalized.

One of the CDC recommendations for preventing transmission of *Salmonella* from reptiles to humans is that reptiles should not be kept in households where children aged <5 years or immunocompromised persons live.(1,2) During 2000, 42% (40 cases) of LAC salmonellosis cases having reptile contact were under age 5 years.

In 2000, one LAC turtle-associated case, a one- month-old infant with *Salmonella* serotype Berta developed *Salmonella* meningitis and septicemia. The turtle was tested and was culture positive for *S*. Berta. A second case, a 2-month-old with *S.* Marina, had no direct exposure to a household pet iguana. The parents were aware of the risk of disease associated with their pet, and tried to take the appropriate precautions, such as restricting the iguana to an area of the home separate from the infant. However, the baby's bottles were washed in the same sink where the iguana's water dish was washed. The iguana was tested and was culture positive for *S*. Marina.

A common misconception is that direct contact with the reptile is necessary to acquire salmonellosis. Indirect contact with a reptile is also a risk; this may include contact with a person who handles reptiles, contact with surfaces where the reptile may have crawled (floors, cages), or

contact with areas where reptile implements such as dishes or aquariums may be washed. Salmonellosis has been reported in infants whose bottles were washed in the same sink where the aquarium was cleaned. Severe complications, including meningitis and death, have occurred as a result of *Salmonella* infections in high-risk individuals such as infants, young children and immunocompromised persons.

Since 1997, LAC ACDC has asked that PHNs in LAC collect specimens for culture from reptiles and their environment whenever the investigation reveals that a reptile resides in the home of a reported case of salmonellosis. These specimens may be collected by either the PHNs or by the owner following instructions provided by the PHN. Table 1 represents 18 LAC salmonellosis cases reported in 2000 in which the reptile tested positive for the same serotype as the human case:

Table 1: Lac Reptile with Same *Salmonella* Serotype as Human Case

Serotype	# of Cases	Reptiles Involved	Comments Re: Human Case
S. Typhimurium	4	Iguana, turtle	3 adults in same household; 4th case: age 11 years
S. Berta	4	Turtles	3 in same household(2 children, age 1 & 4, and adult) 4th case a 1month old infant with positive blood and CSF
S. Newport	2	Iguana, turtle	Index cases: age 2 & 3 years (different households)
S. Infantis	1	Turtle	Index case: age 1 year
S. Marina	1	Iguana	Index case: age 2 months
S. Beaudesert	1	Lizard	Index case: age 2 years
S. SaintPaul	1	Iguana	Index case: age 3 years
S. Singapore	1	Turtle	Index case: age 7 months
S. Urbana	1	Iguana	Index case: age 8 months
S. B:b: Incomplete	1	Dragon Lizard	Index case: age 7 years
S. Java	1	Iguana	Index case: age 47

Reptiles are known to carry multiple serotypes of *Salmonella*, and often shed the organism intermittently without showing any sign of the disease. Unfortunately, attempts to eliminate

Salmonella in reptiles with antibiotics have been unsuccessful. During 2000, the following serotypes were isolated from reptiles that were culture positive for a different serotype than the human case: *S*. Hvittingfoss (lizard), *S*. Newport (snake), *S*. Bardo (tortoise), *S*. Chameleon (iguana), *S*. 58:1,z13,z28:z6 (bearded dragon lizard).

Persons choosing to live with reptiles should be educated about the risk of salmonellosis and provided with the CDC recommendations for preventing transmission of salmonellosis from reptiles to humans. Parents must take responsibility to supervise all children who are exposed to reptiles, and teach them to wash hands thoroughly after handling any reptile.

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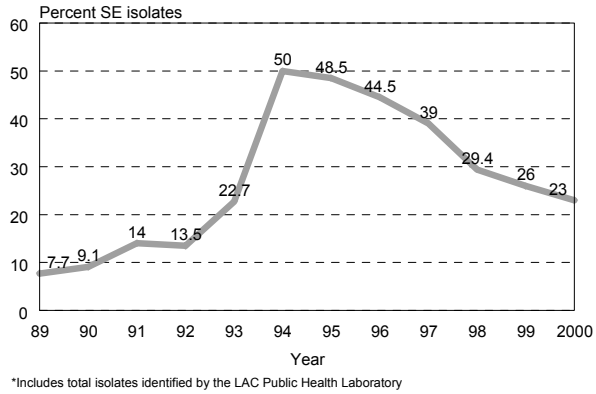
SALMONELLA SEROTYPE ENTERITIDIS IN LOS ANGELES COUNTY, 2000

In the past decade, *Salmonella* serotype Enteritidis (SE) rose steadily from the third most frequent serotype to become established as the most frequently isolated serotype in Los Angeles County (LAC). After rising to a peak in 1994 of 1126 cases, a case-control study of sporadic cases was conducted by the Acute Communicable Disease Control Unit (ACDC) and the California Department of Health Services (1).

Figure 1

Salmonella Enteritidis Proportion of Total Salmonella LAC, 1989-2000



*Includes total isolates identified by the LAC Public Health Laboratory

The case-control study showed a strong association between SE infection and consumption of eggs, especially raw or undercooked eggs. Eating in restaurants also was associated with increased risk of SE infection. The majority of cases occurred in young adults. Since 1994, when 50% of *Salmonella* isolates were SE, SE has gradually decreased proportionally each year, but still remains the most common serotype.

Figure 2

Salmonella Enteritidis Outbreaks

Los Angeles County 1991-2000

SE continues to be the most common *Salmonella* serotype identified from isolates submitted to the Public Health Laboratory. In 2000, SE comprised 231 of 989 (23%) of *Salmonella* isolates serotyped for LAC cases (Figure 1). Of all *Salmonella* isolates, SE represented 50% in 1994 and 26% in 1999 (Figure 1). In 2000, the overall incidence of SE was 2.5 cases/100,000 population compared to 10.7/100,000 for all *Salmonella*.

The highest frequency of SE cases occurred during April, when an outbreak due to unpasteurized orange juice occurred. The usual increase occurred in summer months similar to other *Salmonella* serotypes. SE isolates were identified from feces (89%), followed by

blood (6%), urine (3%), and other/unknown specimens (2%). There were 44 hospitalizations (19%). SE infection was a contributing cause of death in 3 persons with underlying disease (AIDS, cancer).

In 2000, 4/7 (57%) salmonellosis outbreaks were due to SE (Figure 2). One outbreak was part of a multi-state outbreak due to unpasteurized orange juice. The source was unknown for three outbreaks for which investigation was hampered by lack of cooperation by the cases (Table 1).

Table 1. Salmonella Enteritidis Outbreaks in Los Angeles County, 2000

Onset Month	Outbreak Setting	Number Ill	Culture Positive	Phage Type	Suspected Vehicle	Suspected Source
March	Multi -state sporadic cases	17	13	Untype -able	Orange juice	Imported unpasteurized juice
Sept.	Home (catered)	14	1	4	Unknown	Unknown
Oct.	Home	13	4	Untype -able	Unknown	Unknown
Nov.	Home	20	3	4	Unknown	Unknown

ACDC continues to monitor sporadic cases and outbreaks of SE and works with private industry groups and the state and federal governments. ACDC works toward the improvement of egg production, egg distribution processes and consumer education in order to decrease the risk of SE infection.

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SEROPREVALENCE STUDY FOR ANTIBODY TO RATBORNE PATHOGENS AND OTHER AGENTS AMONG SKID ROW RESIDENTS-LOS ANGELES 2000

INTRODUCTION

Rats may be reservoirs in disease transmission. From 1996 through 1998, Norway rats (*Rattus norvegicus*) from downtown Los Angeles were examined for evidence of exposure to certain microorganisms; seroprevalence rates were 25.7% for *Rickettsia typhi*, 6.7% for Seoul Virus (SEOV) and 73.1% for hepatitis E virus (HEV). Fifty-two percent of blood specimens collected from rats grew *Bartonella elizabethae*-like isolates when cultured (Table 1).[1,2] Due to high rat isolate and seroprevalence rates, Los Angeles County Department of Health Services began a blinded study among people using a free clinic in the "skid row" area of Los Angeles for evidence of past exposure to these agents.

Table 1. Overall Seroprevalence and Culture Positive Isolates of Four Agents in *Rattus norvegicus* Captured in Downtown Los Angeles 1996-1998

Agent	% positive
Bartonella elizabethae - like isolate, N = 259	134 (51.7%)
Hepatitis E Virus, N = 134	98 (73.1%)
Rickettsia typhi, N = 259	67 (25.7%)
Seoul Virus, N = 120	8 (6.7%)

METHODS

Between June and August 2000, serum specimens obtained for other routine tests were collected from patients who visited a free clinic on skid row in Los Angeles. Most of these patients had been homeless at some point during the past year (Weingart Clinic, personal communication, 2001). The serum was sent from the free clinic to the Los Angeles County Public Health Laboratory (LACPHL). At LACPHL, three aliquots were drawn off each specimen for testing by 3 different laboratories. LACPHL tested the serum for *Bartonella elizabethae* (BE), *Bartonella quintana* (BQ), *Bartonella henselae* (BH) and *Rickettsia typhi* (RT) antibodies, using reagent provided by the Centers for Disease Control and Prevention (CDC). Antibody to other pathogens not tested for in the rats (*Bartonella quintana* and *Bartonella henselae*) was tested in the human serum.

The National Institutes of Health (NIH) tested the serum for antibodies towards HEV, and Focus Technologies (FT, Cypress, CA) tested the serum for antibodies towards a non-specific Hantavirus panel. Positive tests were later confirmed by CDC for SEOV antibody. Age and sex were the only demographic information collected. No clinical data were collected.

RESULTS

The ratio of men to women was 3:1 with a median age of 41 years. Overall, 25/200 (12.5%) of the specimens had antibody to BE, 19 (9.5%) had antibody to BQ, and 7 (3.5%) had antibody to BH. Thirty (15%) had antibody towards HEV and one (0.5%) had antibody to SEOV (Table 2). None of the specimens had RT antibody. Eighteen percent (35/200) had antibody towards any species of *Bartonella*. Four of the specimens had titers of 1:512 to BQ antigen.

Table 2. Overall Seroprevalence of Antibodies to Six Agents in a Population That Uses a Free Clinic in Downtown Los Angeles, N = (200)

Agent	Seroprevalence, N (%)
*Bartonella elizabethae**	25 (12.5%)
*Bartonella quintana***	19 (9.5%)
*Bartonella henselae***	7 (3.5%)
Hapatitis E Virus	30 (15.0%)
*Rickettsia typhi***	0 (0.0%)
Seoul Virus	1 (0.5%)

* Cutoff = 1:128
** Cutoff = 1:64

DISCUSSION

These data show that humans and *R. norvegicus* living in downtown Los Angeles have antibodies to similar organisms. *R norvegicus* rodents serve as reservoirs of RT, SEOV and possibly BE.

This study found that 9.5% of specimens had antibody towards BQ. Studies conducted in Baltimore, Maryland, Seattle, Washington, and Marseilles and Paris, France, have found homeless populations with a high seroprevalence to BQ.[4-7] BQ is transmitted through the bite of the human body louse (*Pediculus humanus corpis*) and causes trench fever. Donor blood tested in other cities found that 0 to 2% of specimens had antibody towards BQ antigen.[3-5, 7] This may indicate that there is a higher seroprevalence to BQ among the homeless in Los Angeles when compared to donor groups. Four of the specimens had titers to BQ of 1:512, indicative of ongoing or recent clinical illness.

It is not known how BE is transmitted to humans, however, studies suggest that *Rattus norvegicus* may be a suitable reservoir. [2, 8, 9] BE can cause endocarditis[10] There is also one documented case of Leber's neuroretinitis in a patient with serologic evidence of BE.[11] A study done in Baltimore,

Maryland, found that IV drug users had a high seroprevalence rate (33%) to BE.[4] Although our study found a seroprevalence rate of 12.5%, the serologic cutoff used was 1:120. Using a cutoff of 1:64 as the Baltimore study did, the seroprevalence in our study becomes 20%. It is not known how participants may have acquired antibody to BE, but it is interesting that the seroprevalence (comparing the same cutoffs) in Los Angeles was similar to that in Baltimore.

The data show that 3.5% of this population had antibody to BH, the agent of cat-scratch disease. This agent is transmitted through the scratch or bite of a cat and is not known to be transmitted by rodents. The seroprevalence in this population is similar to non-indigent populations. BH usually causes pathology in children more than adults.

None of the specimens tested positive for antibody to RT. RT causes murine typhus and is transmitted by the bite of the rat flea or cat flea. It is known to be endemic in LAC but maintains a more suburban cycle between opossums, cats and humans.[12, 13] The negative findings may be because the rat flea is very rat specific. It does not bite humans unless it cannot find another rat host, as opposed to the cat flea, which will readily bite humans. It might be that with enough rats to feed on, the flea rarely bites human as an alternate host. Therefore, we may not see any evidence of urban murine typhus exposure.

One specimen from the downtown LA population had antibody to SEOV for an overall seroprevalence of 0.5% (1/200). This is remarkable when compared with the seroprevalence of two populations studied in Baltimore Maryland, which had a seroprevalence of of 0.16% and 0.25% in IV drug users and people with no known risk factors, respectively.[14,15] SEOV is a Hantavirus and is rodent-borne, through the urine or feces of the Norway rat. It can cause hemorrhagic fever with renal syndrome (HFRS). Seroprevalence to Baltimore rat isolate of SEOV was 44% in Norway rats captured in Baltimore, Maryland. A study in Baltimore found that 2.76% of a group of dialysis patients with end-stage renal disease had antibody to a strain of SEOV. The same study also found that 6.5% of patients with renal disease due to hypertension were seropositive for antibodies towards this same virus, suggesting that SEOV may be associated with renal disease.[16]

HEV is transmitted through the fecal-oral route and has been implicated in many epidemics in the Third World. It causes acute hepatitis and can cause death in pregnant women. It is not known how HEV antibody is acquired in this population or whether rodents and humans were infected with the same strain.

Clinicians who serve homeless populations should be aware of potential patient contact with rodents and possible subsequent infection. Further studies and similar surveys in age-matched groups are needed to determine if exposure to rodents may be associated with clinical illness in this population.

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VARICELLA ACTIVE SURVEILLANCE PROJECT 2000

BACKGROUND

The Varicella Active Surveillance and Epidemiologic Studies in Antelope Valley was funded by the Centers for Diseases Control and Prevention(CDC) in September 1994 to (1) develop a reporting system to accurately define the baseline incidence and epidemiological profile of varicella disease prior to licensure and widespread use of varicella vaccine, (2) identify changes in the epidemiology of varicella as a result of vaccine usage, (3) ascertain the immunization status of cases, and (4) evaluate the demographic and clinical profiles of vaccinated and unvaccinated cases of varicella.

The Antelope Valley is located in the northeastern part of Los Angeles County (LAC) and consists of approximately 35 communities, covering nearly 2,000 square miles. Sixty-three percent of Antelope Valley's population of approximately 300,000 reside in its two largest cities, Lancaster and Palmdale. The racial/ethnic composition of the population in 2000 was estimated to be 63% White, 24.3% Hispanic, 6.4% Black and 5.2% Asian/other. In 1998, there were approximately 5,000 live births in Antelope Valley. The area's relative isolation from other large urban centers encourages the use of local medical providers and facilities. Both the geographical location and relatively young age distribution of Antelope Valley residents has made it an ideal study site.

METHODS

The population-based varicella active surveillance project (VASP) collects reports of varicella from 305 surveillance units, which represent nearly all potential surveillance units identified; these include all public and private schools and day care centers with enrollments of 12 or more children; public health clinics, hospitals, private practice physicians, and health maintenance organization (HMO) offices; employers with 500 or more employees; correctional facilities; and miscellaneous others likely to identify and report cases of varicella. A case of varicella is defined as illness with an acute onset of a diffuse papulovesicular rash without other known cause. Case reports and data regarding vaccine administration are collected every two weeks. A structured telephone interview is conducted with each case or parent/guardian to collect detailed demographic, clinical, and health impact data and to determine if there are additional cases or susceptible contacts within the household. Susceptible household contacts are re-interviewed four to six weeks after the initial contact to identify additional cases. Only cases that are confirmed by case interview are counted as verified. Those that are unreachable by telephone or decline the interview are considered probable cases. Data collection began January 1, 1995.

In September 1995, the project began to monitor vaccine use in the study population. A varicella immunization report is submitted monthly by all 59 providers currently offering the vaccine. Herpes zoster was included in active surveillance beginning January 1, 2000. Case interviews are only conducted on reported cases of herpes zoster aged 19 and younger.

REPORTING SOURCES

A total of 281 reporting sites representing 305 surveillance units are currently participating (Table 1). Varicella cases also are identified through household interviews and occasionally from sources not specifically under active surveillance. Fluctuation in the number of surveillance units by type are primarily related to schools, day care centers and medical facilities opening, consolidating, or closing. No sites have refused further participation in the project. With prompting, reporting site compliance in submitting case logs every two weeks to the VASP office is 100%.

Table 1. Participating Surveillance Units, Antelope Valley, VASP, 1995, 1999, and 2000

	Number and Distribution of Surveillance Units Participating		
Surveillance Unit by Type	1995 N (%)	1999 N (%)	2000 N (%)
Elementary and High Schools	93 (32.7)	101 (32.7)	102 (33.9)
Preschool/Day Cares	49 (17.2)*	76 (24.6)	76 (24.9)
Private Practice MDs	89 (31.3)	81 (26.2)	73 (23.9)
HMO Offices	7 (2.5)	19 (6.1)	20 (6.6)
Hospitals	4 (1.4)	3 (1.0)	3 (1.0)
Public Health Clinics	12 (4.2)	11 (3.6)	13 (4.3)
Correctional Facilities	3 (1.0)	3 (1.0)	3 (1.0)
Large Employers	11 (3.9)	10 (3.2)	10 (3.3)
Miscellaneous	14 (4.9)	3 (1.0)	3 (1.0)
Households	1 (0.4)	1 (0.3)	1 (0.3)
Outside Normal Sampling	1 (0.4)	1 (0.3)	1 (0.3)
TOTAL	284 (100)	309 (100)	305 (100)

VARICELLA SURVEILLANCE DATA

Between January 1 and December 31, 2000, surveillance units reported 1,008 persons with varicella; 82 (8.1%) were excluded when case interviews revealed that illness or school absence

was not due to varicella, 837 (83.0%) were verified by telephone interview and collection of clinical data was completed, 89 (8.8%) were unreachable by telephone or declined to be interviewed and were considered probable cases, and none are pending collection of clinical data. In this report, analysis is limited to verified cases unless otherwise specified.

In 1995, unvaccinated first varicella cases comprised 95% of total verified varicella cases; however, in 2000 they now comprise 74% of cases. This decrease was largely influenced by breakthrough cases (varicella infection >42 days after vaccination) (Table 2).

Table 2. Verified Varicella Case Type, Antelope Valley, VASP, 1995, 1999 and 2000

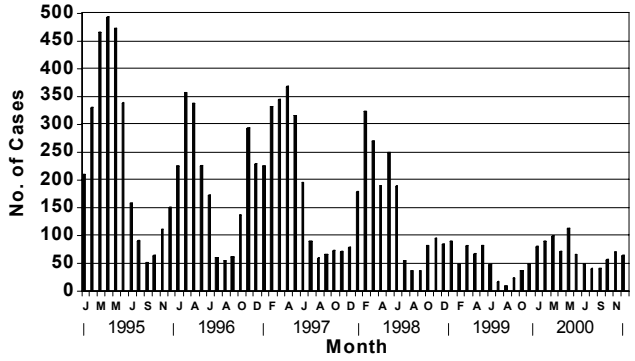
Verified Varicella Case Type	1995 N=2,934 n (%)	1999 N =587 n (%)	2000 N=837 n (%)
Possible Breakthrough Cases (Onset >42 days after vaccination)	4 (0.1)	52 (8.9)	141 (16.8)
Reported Second Infections (Reinfections)	132 (4.5)	78 (13.3)	81[1] (9.0)
First Infections, Unvaccinated ("Classic" Disease)	2,798 (95.4)	457 (77.8)	620 (74.0)

[1]Of the 81 cases, 5 cases experienced both a breakthrough and reported a previous history of varicella.

Trends

The number of verified varicella cases declined 80% between 1995 and 1999 (2,934 and 587 cases in 1995 and 1999, respectively), but increased 43% to 837 cases in 2000. A blunting of characteristic seasonality was noted in 1999 and, to a lesser extent, again in 2000 (Figure 1).

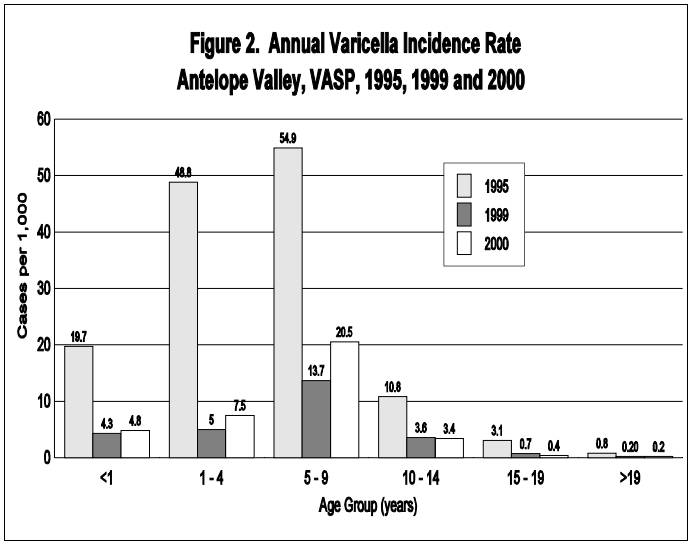
Figure 1. Verified Varicella Cases by Month of Onset, Antelope Valley, 1995-2000



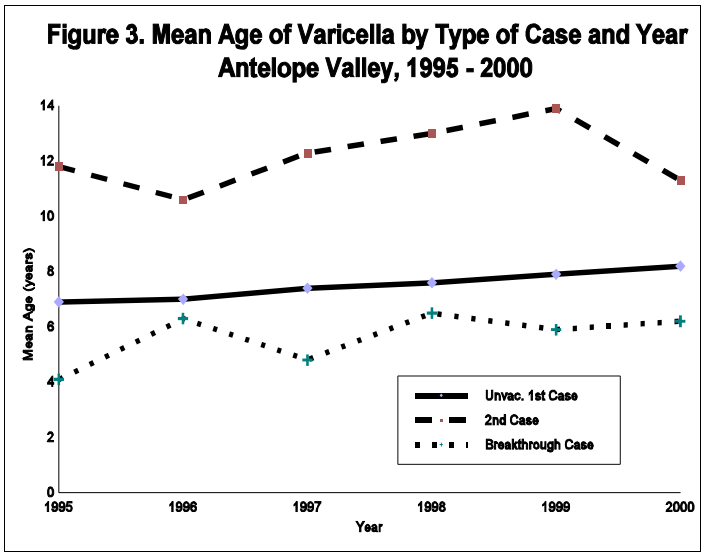
Age

Rates decreased in all age groups over the study period but the decline was most pronounced among children aged one to four years. In 2000, rates were highest among children aged five to nine years (20.5 per 1,000 population), followed by children aged one to four years (7.5 cases per 1,000), and children aged less than one year (4.8

per 1,000) (Figure 2). The increase in 2000 compared to the previous year was largely explained by increases among children aged five to nine years (50% increase) and one to four years (50%).



The overall mean age of verified cases was 7.1 years in 1995, 8.5 years in 1999 and 8.1 years in 2000. Limiting the analysis to unvaccinated first cases (excluding the breakthrough and reinfections), the mean age was 6.9 years in 1995 and 8.2 years in 2000 (Figure 3). The mean age of breakthrough cases and second infections in 2000 was 6.2 years and 11.3 years, respectively.



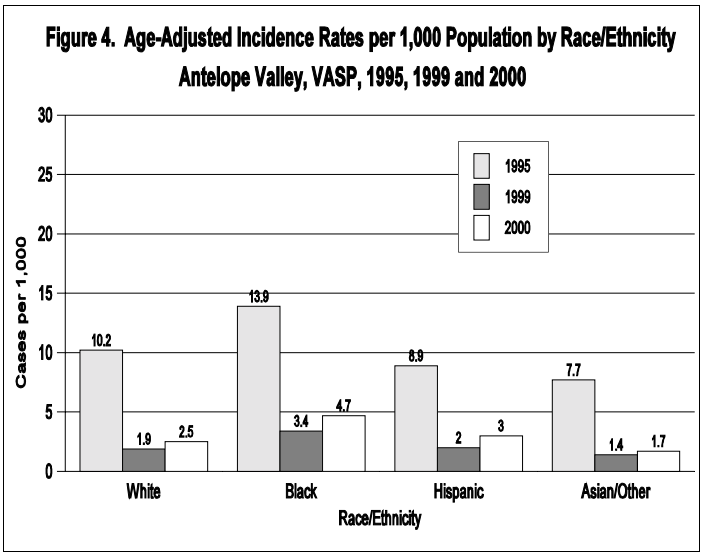
Gender

In 1995, there was considerable variation in the female:male case ratio by age group, with females aged 20 years and older outnumbering males of the same age group 1.6:1; in 2000, the female-to-male case ratio approximated 1:1 in all age groups.

Race/Ethnicity

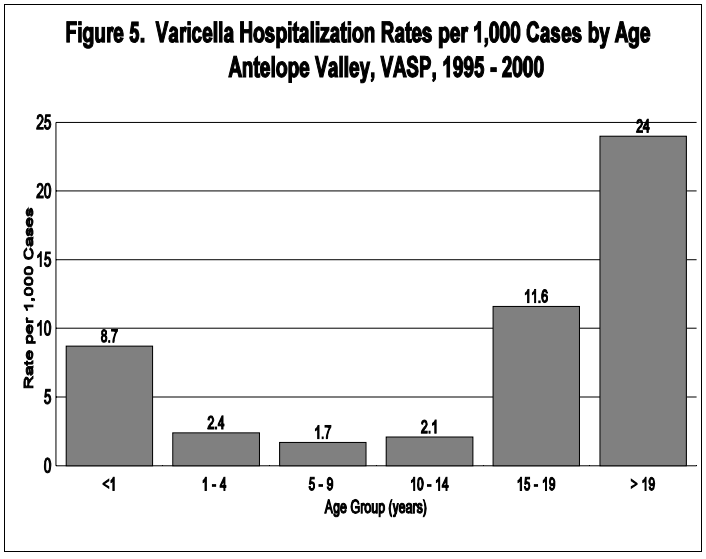
As in previous years, age-adjusted incidence rates of varicella among Blacks were higher than among non-Hispanic Whites (Figure 4). In 2000, Black children aged five to nine years experienced the highest rates of any racial/ethnic group (26.7 cases per 1,000 population). This rate is higher than the 19.8 cases per 1,000 reported in 1999 (data not shown). Higher than anticipated rates of varicella among Blacks may be the result of underestimation of the number of Black residents in the Antelope Valley; data from the California Basic Educational Data System (CBEDS) suggest that the number of school-aged Black children in the Antelope Valley is substantially higher than the Antelope Valley

population estimates compiled by County of Los Angeles Internal Services Urban Research Division.



Lesion Severity

Beginning January 1, 1997, along with the two other project sites, we modified the definition of lesion grading from "mild" (<50), "moderate" (50-250) and "severe" (>250) to "less-than-average" (<50), "average" (50-500) and "more-than-average" (>500). The definition of <50 lesions for "mild" cases in 1995 and 1996 changed only in name to "less-than-average" in 1997. Thus, the mildest lesion grading definition remained consistent from 1995 to 2000. The proportion of case patients with a "more-than-average" lesion grading decreased from 9.2% in 1997 to 6.2% in 2000 (χ^2 =6.85, p<0.01). In 1999 and 2000, the proportion of cases with "more-than-average" lesion grading was highest among 15- to- 19-year-olds. Across all age groups, there was a trend towards milder lesion grading over the six-year study period. As in previous years, lesion severity in breakthrough cases in 2000 was significantly milder than in cases that were unvaccinated experiencing their first varicella infection (χ^2 =75.86, p<0.005): 78% of breakthrough cases reported "fewer-than-average" lesions, compared with 37.6% of unvaccinated first varicella cases.



Severity of Disease Index

In 2000, 92.4% of cases reported a Severity of Disease Index (SDI) of 1, indicating mild uncomplicated disease, compared with 84.1% in 1995 (χ^2=38.7, p<0.005). Only 2 (0.2%) cases reported an SDI > than 2. In 2000, adults were more likely than other age groups to have complications (SDI 2), although this finding may be biased due to small numbers (Figure 6). Severity of Disease Index for breakthrough cases in 2000 did not differ significantly from unvaccinated first varicella cases. Beginning in January

2000, case-patients/parents were asked to subjectively assess their illness. Forty percent were described as "not appearing sick," 45% were "moderately sick," and 14% were "severely sick." Adults were significantly more likely to be assessed as "severely sick" (χ^2=35.9, p<0.005).

Complications

We defined a complication as a self-reported condition or event for which the case-patient was evaluated and treated by a health care provider and which occurred within two weeks of the onset of varicella disease. Self-reports of complications were confirmed for hospitalized cases only. Of the 837 verified cases in 2000, 50 (6%) cases reported 59 complications. Fewer cases reported complications in 2000 than in any previous year (compared with 13% in 1995, 8% in 1996, 10% in 1997, 11% in 1998, and 10% in 1999).

There were only two varicella-related hospitalizations in 2000. One patient was a vaccinated four-year-old White male with onset of varicella on January 28, 2000, who was hospitalized for two days beginning January 30 with acute bronchospasm and associated dyspnea/hypoxia. The second was a five-year-old Hispanic male with onset of varicella on January 3, 2000, who was hospitalized on January 13 status post cardiopulmonary arrest due to an asthmatic attack. This child suffered permanent brain damage as a result of this episode. The rate of hospitalization due to varicella was lower (0.6/100,000 population) in year 2000 than in any previous year. Considering combined years 1995-2000, adults aged 19 years and older had the highest rate of hospitalizations (24 per 1,000 varicella cases), while children aged 5 to 9 years had the lowest rate (1.7 per 1,000 cases) (Figure 5).

Medications Received During Varicella

Cases receiving antiviral medication increased from 4.7% of reported cases in 1995 to 8.6% in 2000 (χ^2 =18.8, p<0.005), ibuprofen use increased from 3.8% of cases in 1995 to 13.1% in 2000 (χ^2 =49.9, p<).005), while antibiotic use decreased from 12% of cases in 1995 to 6.2% in 2000 (χ^2 =23.2, p<0.005).

Varicella Outbreaks

An outbreak was defined as 5 or more cases reported from the same school or daycare within a 21-day period, continuing until such time as a 21-day period occurred without a reported case. While the number of outbreaks decreased 67% from 58 in 1995 to 19 in 2000, the number of outbreaks increased 2.7 fold from 7 in 1999 to 19 in 2000 (Table 3). Of the 62 cases comprising the 7 outbreaks in 1999, 3 (4.8%) cases were among vaccinated and 59 (95.2%) were among unvaccinated individuals. Of the 226 cases that comprised the 19 outbreaks in 2000, 47 (20.8%) cases were among vaccinated and 179 (79.2%) were among unvaccinated individuals.

Table 3. Varicella Outbreaks, Antelope Valley, 1995, 1999, and 2000

Varicella Outbreaks	1995*	1999	2000
Total No. of outbreaks	81	20	34
Total No. of cases in outbreaks	1,332	174	356
Average No. of cases/outbreaks	16.4	8.7	10.5

*1995 data exclude cases ascertained from other reporting sites and thus represent an underestimate

Breakthrough Disease

We defined breakthrough disease as a reported case of varicella that occurred in a person who had received varicella vaccine more than 42 days before rash onset. Varicella vaccination was confirmed in one of two ways: (1) interviewees checked the vaccine immunization record at the time of the telephone case interview, or (2) medical office staff (who reportedly administered the vaccine) checked the medical record. Of 837 verified cases of varicella in 2000, 164 (19.6%) cases occurred in persons who reported having received varicella vaccine. Of these, 141 (86%) developed varicella 42 or more days after vaccination and were considered possible breakthrough cases. Breakthrough cases as a proportion of total cases increased each year in all age groups. In 2000, 25.4% of cases in children aged 1 to 4 years, 18% of cases in children aged 5 to 9 years and 9.5% of cases in children aged 10 to 14 years were classified as breakthrough cases.

In 2000, most of the breakthrough cases had fewer than 50 lesions (78%) and the vast majority (94%) had no complications (severity of disease index 1). More than 76% of the breakthrough cases had a known source of exposure to varicella and nearly half (47.5%) were diagnosed by a healthcare provider (Table 4). The average interval between the date of vaccination and onset of breakthrough varicella in the 351 cumulative breakthrough cases (1995-2000) was 1.9 years. This interval increased from 2.1 years for the 52 cases in 1999 to 2.7 years for the 141 cases in 2000.

Table 4. Breakthrough Varicella Cases (Occurring >42 days After Receipt of Varicella Vaccine), Antelope Valley, 1996, 1999 and 2000

Age, Confirmation of Vaccination, Lesion Grading, Disease Severity, Illness Order, Source of Varicella Exposure and Source of Varicella Diagnosis		1996 N=24 n (% of cases)	1999 N=51 n (% of cases)	2000 N=141 n (% of cases)
Age:	1-4 Years	12 (1.6)	20 (16.0)	49 (25.4)
	5-9 Years	10 (0.8)	27 (9.0)	82 (18.0)
	10-14 Years	1 (0.5)	4 (4.6)	8 (9.5)
	15 - 19 Years	0	0	0
	> 20 Years	1 (0.8)	0	2 (4.0)
Confirmed Receipt by:	Vaccine Record	N/A	10 (19.6)	42 (29.8)
	Healthcare Provider	N/A	31 (60.8)	71 (50.4)
	Recall only	24 (100)	8 (15.7)	14 (9.8)
Lesion Grading:	<Average	17 (70.8)	39 (76.5)	110 (78.0)
	Average	7 (29.2)	11 (22.6)	29 (20.6)
	>Average	0	1 (2.0)	2 (1.4)
Disease Severity:	Index 1	20 (83.3)	48 (94.1)	132 (93.6)
	Index 2	4 (16.7)	3 (5.9)	8 (5.7)
	Index 4	0	0	1 (0.7)
Illness Order:	Primary or Co-Primary		45 (88.2)	129 (91.5)
	Secondary		6 (11.8)	12 (8.5)
Sources of Varicella Diagnosis:	Healthcare Prov.	8 (33.3)	26 (51.0)	67 (47.5)
	Parent/Self	16 (66.7)	25 (49.0)	74 (52.5)
	Other	0	0	0
Source of Varicella Exposure:	Known Source[1]	21 (87.5)	28 (54.9)	108 (76.6)
	Unknown	3 (12.5)	23 (45.0)	33 (23.4)
Receipt of other Vaccines on the Same Day as Varicella		2 (8.3)	22 (43.1)	Not ascertained

Days of School and Work Missed Due to Varicella

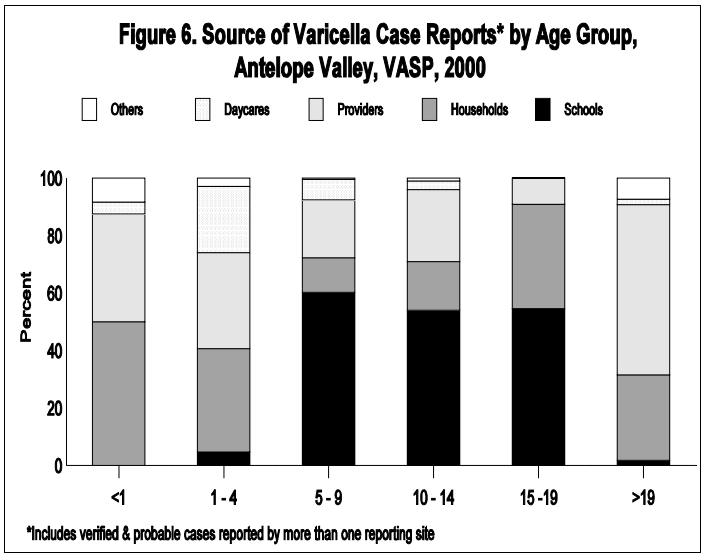
The total number of days of school or work days missed by cases and caretakers decreased 80% from 14,842 days in 1995 to 2,906 days in 1999, then increased 55% to 4,486 days in 2000. The mean and median number of days of school or work missed by cases and caretakers have remained relatively constant from 1995 to 2000 (data not shown).

Suspected Source of Varicella Infection

Schools were the suspected source of infection for 32.7% of the cases, followed by households for 29.4%. The number of cases reported with "unknown" source of infection decreased from a high of 28.6% in 1999 to 22.6% in 2000. In both 1999 and 2000, adults reported the highest percentage of "unknown" exposure source.

Source of Report

In 2000, as in previous years, more cases were reported from schools than from any other surveillance unit type (40.5% of all cases were reported by schools). For the first time, in 2000, healthcare providers reported more cases (26.1%) than were ascertained from households of cases being interviewed (20.7%). In 2000, adults were reported by healthcare providers (50.8%) than through household interviews (25.4%). Infants and children aged less than four years were reported primarily by households, and school-aged children (aged five to nineteen years) were reported primarily by schools (Figure 6).



Source of Diagnosis

Over the study period, an increasing proportion of cases was diagnosed by healthcare providers (16.3% in 1995 compared with 41.9% in 2000). In 2000, the proportions of second varicella cases and breakthrough cases diagnosed by a healthcare provider were 56.6%, 47.5%, and 38.9%, respectively.

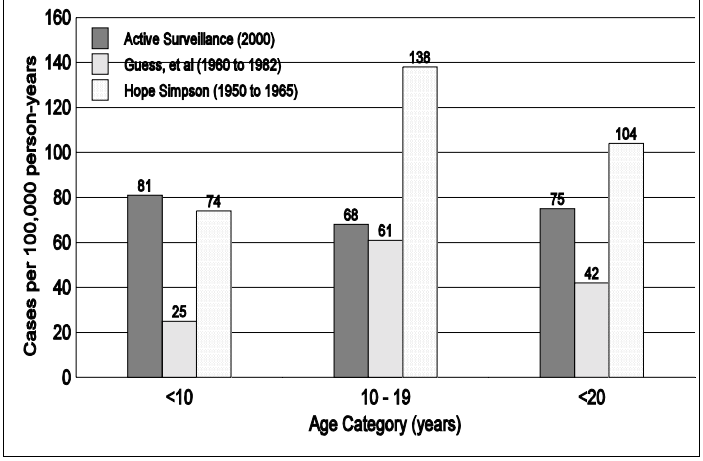
Second Varicella Infections

In 2000, 81 (9.7%) cases reported a history of previous varicella; the mean age at first infection was 3.3 years and at second infection was 10.1 years. Since second cases of varicella have been sporadically reported, the VASP surveillance project provided the opportunity to look more closely at reported occurrence of varicella reinfections. We collaborated with CDC to describe the epidemiology and clinical characteristics of varicella reinfections reported to the surveillance project. From January 1995 through December 1999, 740 (7.3%) cases reported a prior varicella infection. Of 135 cases of varicella with onset between January through September 1998 with history of disease, 98 were reinterviewed. Reinfection cases were younger at 1st infection (3 years) and older at 2nd (8 years) than those with only one infection (6 years). Second infections increased from 4.5% of reported cases in 1995 to 13.3% in 1999. There were no gender or race/ethnicity differences and all cases with multiple infections occurred in healthy persons and tended to cluster in families. Eleven percent experienced complications for which they consulted a healthcare provider. Although the data from this study must be interpreted with caution since we had no laboratory confirmation of either first or second infections, we concluded that (1) reinfections are more common than previously thought; (2) second infections tended to occur in persons whose first infection was exceptionally mild and occurred at a young age; and (3) first infections did not act like vaccine, as most reinfections were average or severe cases of disease.

HERPES ZOSTER SURVEILLANCE

Between January 1 and December 31, 2000, surveillance units reported 320 persons with herpes zoster; nine were duplicates and one was incorrectly reported. The number of reported cases ranged from 16 to 36 cases per month. There was no apparent seasonality. The majority of the cases were diagnosed by a healthcare provider, but no confirmatory testing was obtained. Additional clinical and demographic variables were collected from cases aged less than 20 years during a telephone interview using a structured questionnaire.

Figure 7. Comparison of Crude Incidence Rates of Herpes Zoster (Cases/100,000 person-years)



Age

Of 309 herpes zoster cases, 77 (25%) cases occurred in persons aged less than twenty years, and 788 (25%) cases occurred in adults aged 70 years and older. Four (1.3%) cases occurred

among vaccinated children aged less than five years. The crude incidence rate (without adjusting for prior history of varicella) was 81 cases per 100,000 population for children aged less than 10 years, 68 cases per 100,000 population for children aged 10 to 19 years, and 75 cases per 100,000 population for adults aged 20 years and older. A comparison of these rates and others published in the literature are shown in (Figure 7).

Comparison of herpes zoster rates, especially among children, in different studies and populations are not very meaningful because of differences in study methodology as well as differences in the proportion of children with prior varicella and no vaccination experience. Ascertainment and classification bias also must be addressed before meaningful comparisons can be made.

Race/Ethnicity

The racial/ethnic distribution of the 309 HZ cases is as follows: 186 (60.2%) White, 44 (14.2%) Hispanic, 15 (4.9%) Black, 6 (1.9%) Asian/Other, and 58 (18.7%) unspecified or unknown. The 77 HZ cases in individuals aged <20 years, for which data are most complete, had a racial/ethnic distribution as follows: 50 (88 cases per 100,000 population) White, 17 (56 cases per 100,000 population) Hispanic, 3 (39 cases per 100,000 population) Black, 3 (73 cases per 100,000) Asian/Other, and 4 (5.1%) unspecified or unknown.

HZ in Children and Adolescents Aged Less Than 20 Years

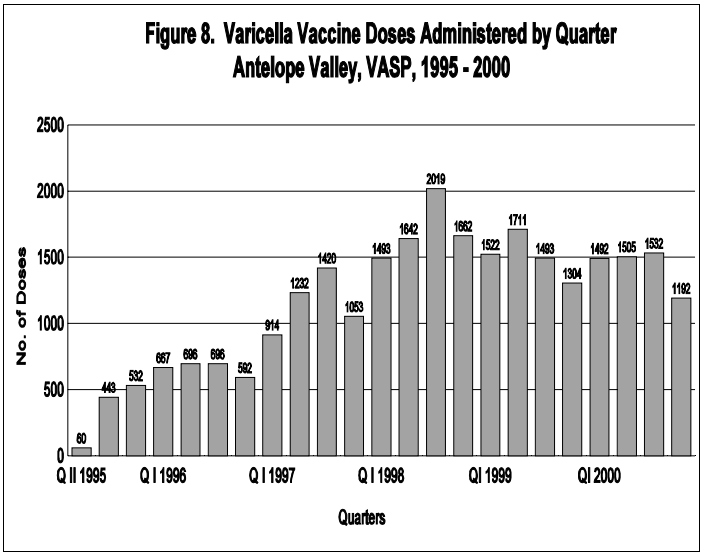
Of the 75 cases of HZ in unvaccinated individuals aged less than 20 years, 68 (93%) were available for the interview. Of these, 67 (99%) were diagnosed by a physician and 1 (1%) was diagnosed by a school nurse. The mean age of these cases was 11 years; 59% had varicella before age four years. The average time between varicella and HZ was nine years.

The estimated diameter of the HZ rash was less than one inch for 10 cases (15%), one to three inches for 48 (71%), four to six inches for eight (12%), and more than six inches for two (3%). Pain levels were assessed as none, mild, moderate, severe, or excruciating. Overall, pain severity averaged moderate with mean duration of 7.4 days among the 56 cases that experienced pain. Pain or paresthesia (burning, itching) was the initial symptom prior to the appearance of the HZ rash in 33 (49%) cases. The majority of cases (74%) involved the thoracic dermatomes, followed by cervical and then lumbar.

Forty-two cases (62%) reported 221 missed days of school or an average of 5.3 days (range 1-30 days). Thirty-one (46%) cases received acyclovir and 11 (16%) took prescription pain medication. The rash was localized to one dermatome in 60 (88%) cases and involved two or more dermatomes in 8 (12%). Rash duration was less than four weeks for 45 (66%) cases, four to eight weeks for 19 (28%), and more than eight weeks for 3 (4%). Residual scarring was reported by 26 (38%) cases. Postherpetic neuralgia (PHN) was reported by 6 (9%) cases; PHN lasted less than two weeks for four cases and a month or longer for two cases. Interviewees cited stress as a

possible contributing factor (e.g., death of a household member, parental divorce, school, etc.) prior to HZ occurrence in 22 (32%) cases.

Four cases of HZ were reported in vaccinated children aged less than five years with an average interval of 2 years (range 10 months to 38 months) between vaccination and occurrence of HZ. No laboratory testing was performed to confirm the diagnosis or to determine the virus strain associated with these cases. Three of the four cases were reported by healthcare providers and one case by a school surveillance unit. Vaccination dates were all confirmed by the healthcare providers administering the vaccine.



VARICELLA VACCINE UTILIZATION

Fifty-nine reporting sites were providers of varicella vaccine in 2000, compared to forty-seven in 1999. Reporting site compliance with returning the monthly immunization report to the VASP office during 2000 was 100%. The number of administered vaccine doses leveled off in 2000 after increasing each preceding year since vaccine licensure in 1995 (Figure 8). One-year-olds represent the largest proportion of vaccine recipients (3,251; 57%) in 2000. Health Maintenance Organizations (HMOs) provided 2,160 (37.8%) of the vaccine doses administered in 2000, followed by private practice healthcare providers (1,880; 32.9%) and Los Angeles County public health clinics and Medi-cal providers (1,681;29.3%).

EVALUATION

Reporting Completeness

Capture-Recapture

We estimated (1) the number of varicella cases among children two to eighteen years of age missed by the surveillance system and (2) the true number of varicella cases in that same age group, by analyzing the degree of overlap between two incomplete lists of cases (two-source capture-recapture methods). The two ascertainment sources used were 'schools' (elementary, middle and secondary schools, preschools, and daycare facilities), and 'healthcare providers' (physicians, clinics, hospitals, and health maintenance organizations). We limited the analysis to children two to eighteen years of age to decrease heterogeneity of the two ascertainment sources;

fewer than 10% of children under two years of age in the study population attend a child care facility with an enrollment of 12 or more (data not shown).

In this model, *a* is the number of cases reported by both sources, *b* is the number of cases reported by source x only, *c* is the number of cases reported by source y only, and *d* is the number of cases missed by both ascertainment sources. In our calculations we included an adjustment for small samples that yields a nearly unbiased estimator (NUE) for unascertained cases and total cases in the population, as described by Wittes et al.,[1] and Hook and Regal.[2]

Thus, the nearly unbiased estimator of total cases in children aged two to eighteen years not ascertained by school or providers (d_{nue}) is given by $(bc)/(a+1)$, and the total cases in the population with varicella in this age group (p_{nue}) is given by $[(a+b+1)(a+c+1)/(a+1)]-1$.

We evaluated possible within-source variation in probability of ascertainment by stratifying by age, race, and overall disease severity. We calculated 95% confidence intervals for p_{nue} using goodness-of-fit. Using only two ascertainment sources, we estimate 55% completeness during 2000 in the two- to eighteen-year-old age group. Considering cases from all surveillance units, including those outside the selected ascertainment sources (i.e., households), overall completeness of surveillance data for this age group was 67%, down from 74% in 1999.

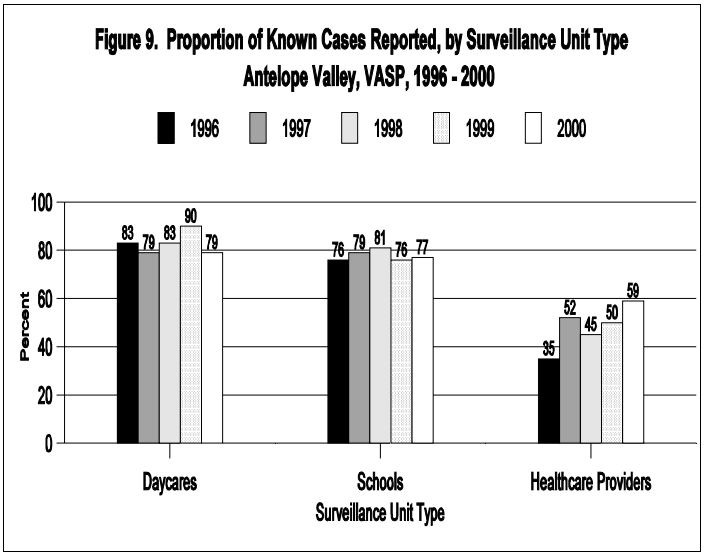
Underreporting of Known Cases

This method of estimating underreporting focuses on those cases in all age groups that were known to, and should have been reported by, surveillance units (pre-schools/daycares, schools and healthcare providers). To obtain this information, the Varicella Case Report form contains an Underreporting Survey which includes the following questions:

- Did case attend preschool? If yes, specify: _____
- Did case attend daycare? If yes, specify: _____
- Did case attend school? If yes, specify: _____
- Did case consult a healthcare provider by telephone? If yes, specify:_____
- Did case see a healthcare provider in the office? If yes, specify: _____
- Was case out of session (off-track, summer break, spring break, etc.) when case had varicella?

After collecting the responses to the above questions, varicella surveillance staff determine whether or not the specified preschool/day care, school or healthcare provider is a surveillance unit. Under-reporting by surveillance units can be estimated by ascertaining whether or not the case was known to surveillance units other than the one that initially identified (or reported) the case.

The Varicella Surveillance Project (VSP) began collecting this information June 1, 1996. Generally, this study shows that schools, daycares and healthcare providers report 66% of the varicella cases they encounter. Specifically, daycare reporting ranges from 79% to 90%, schools from 76% to 81% and healthcare providers 35% to 59% of the cases they encounter. Reporting by healthcare providers increased by 4% in 2000 compared to 1999 (Figure 9).



SPECIAL STUDIES

Varicella Vaccine Coverage and Disease Susceptibility Survey

Since there is evidence of herd immunity in the VASP surveillance sites, it will be increasingly important to monitor disease susceptibility and true vaccine coverage in adolescents. As disease declines, an increasing number of older children may not be exposed to infection. The objectives of this survey are (1) to determine the proportion of adolescents who do not have a history of varicella, (2) to determine proportion of adolescents who have been vaccinated and, if needed, (3) to offer varicella vaccine to susceptible adolescents. The single-page survey (in English and Spanish) was given to Antelope Valley middle school parents/guardians through the school health office. As of the writing of this report, 3,996 surveys have been returned to VASP and entered into a database; approximately 600 are pending entry. Of the 3,996 surveys, 3,440 (86.1%) report a prior history of varicella, 469 (11.7%) report a negative history and 87 (2.2%) were unknown. Of the 469 reporting a negative history, 165 (4.1%) report vaccination and supply a date of vaccination after 1995. The percentage of susceptibles is in the range of 5.7% to 7.5%. The racial/ethnic distribution of respondents was 535 (13.4%) Black, 1,906 (47.7%) White, 1,192 (29.8%) Hispanic, 287 (7.2%) Asian/other, and 76 (1.9%) not answered. Figure 17 compares the racial/ethnic distribution of respondents to the 1997 Antelope Valley census projections and CBEDS 2000/2001. Complete analysis of varicella vaccine coverage and disease susceptibility survey is forthcoming pending entry of remaining surveys.

Laboratory Confirmation of Varicella Disease

Since an increasing proportion of varicella cases are occurring among vaccinees, the validity of clinical diagnosis has been raised. In addition, it is increasingly important to identify atypical varicella disease of any severity and also confirm whether adverse events following vaccination are

related to vaccine virus or wild virus. By offering free laboratory testing to all physicians in the active surveillance sites, we can examine the validity of a clinical diagnosis compared with PCR testing, IgM, and acute and convalescent IgG tests. The objectives of this study are (1) to provide serology testing to confirm suspected cases of breakthrough varicella in vaccinated individuals, (2) to provide serology testing to confirm suspected cases of varicella in individuals presenting with typical or atypical varicella and a prior history of disease, (3) to provide serology testing of adolescents and adults with a negative history of varicella or for any person with an uncertain history of varicella, and (4) to provide serology testing for suspected adverse events related to varicella vaccination.

The availability of CDC Varicella Zoster Laboratory services was presented in the Varicella Newsletters sent to every healthcare provider (HCP) in the Antelope Valley (AV) three times in 2000. A separate mailing describing the laboratory services in detail was sent to all AV HCPs in September of 2000. In November a dinner meeting for all HCPs was held to address the results of VASP to date and the availability of free laboratory testing. Approximately 60 health care providers attended the meeting and a description of the availability of laboratory testing was distributed to those present. Early in 2001, laboratory testing kits were distributed to AV HCPs who appeared to express special interest in laboratory testing.

Prior Varicella Study

Over a four-year period, varicella case-patients reporting a previous history of varicella increased two-fold, from 4.5% in 1995 to 9.5% in 1998. In order to describe the epidemiology and clinical characteristics of varicella reinfections reported to VASP, we re-interviewed 102 case-patients from 1998, obtaining a more detailed description of first and second varicella infections. In collaboration with the CDC, our analysis of the data suggests that clinical varicella reinfections may occur more commonly than previously thought. A paper of the results, “Second varicella infections: are they more common than previously thought?,” is being submitted for publication.

COMMENTS

After six full years of data collection, the project has demonstrated substantial decrease in the number of varicella cases in the Antelope Valley. The Antelope Valley site is currently the only varicella active surveillance site that includes all potential sampling units within a reporting site, thus avoiding problems of sampling error. Large amounts of data have been collected on the epidemiology of varicella pre- and immediate-post vaccine licensure. Further reduction of morbidity and complications from varicella are expected to continue as vaccine coverage increases. California has passed legislation to require proof of varicella immunity at kindergarten entry as of July 2001. Such school laws are expected to further impact the epidemiology of the disease.

Baseline data on incidence of varicella and vaccine coverage levels in Antelope Valley have now been established. With this background, further questions on the disease and vaccine can be

developed as coverage rates increase. Investigation of vaccine breakthrough cases and failures will continue to be of interest, and may not only involve clinical description of such cases, but viral characterization as well. Another important issue is the potential serious morbidity as a cohort of the children who were not vaccinated as infants reach adolescence. Likewise, more information is needed on the impact of routine varicella immunization in the incidence of herpes zoster. Maintaining active surveillance of epidemiology of varicella clearly remains a public health priority.

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