

Acute Communicable Disease Control

Special Studies Report

2001



**County of Los Angeles
Department of Health Services**

Public Health

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OUTBREAK OF INVASIVE ASPERGILLOSIS AMONG RENAL TRANSPLANT RECIPIENTS*

ABSTRACT

Background: Invasive aspergillosis occurs most commonly among patients who are severely immunocompromised; it is rare among renal transplant recipients. During January-February 2001, four cases of invasive aspergillosis among renal transplant recipients in a local hospital where construction activities were ongoing were reported to Acute Communicable Disease Control.

Methods: To determine risk factors for invasive aspergillosis, cohort, environmental, and laboratory studies were conducted among all renal transplant recipients who were hospitalized for any reason between January 1 and February 5, 2001.

Results: Four cases occurred among 40 renal transplant recipients hospitalized during the study period. Three additional cases occurred subsequently. A review of environmental precautions during construction revealed lapses in compliance with established policies and procedures for protection of patients at high-risk for invasive aspergillosis. The use of the anti-rejection agent sirolimus, alone or with mycophenolate, was associated with increased risk for developing invasive aspergillosis.

INTRODUCTION

Invasive aspergillosis usually occurs among severely immunocompromised patients, such as stem cell transplant recipients, those with prolonged neutropenia, and those undergoing treatment for graft versus host disease [1]. The mortality rate ranges between 68% and 100%. The most commonly isolated species, *Aspergillus fumigatus*, causes approximately 90% of human infections and is ubiquitous in the environment. Infection follows inhalation of spores. Pulmonary infection is the most common form of invasive disease, but infection of the sinuses as well as dissemination to the central nervous system, heart, gastrointestinal tract, bone, skin, and other sites also may occur [2]. Although the incidence can be up to 15% among bone marrow transplant recipients, it is less common among solid organ transplant recipients and very rare among renal transplant recipients; outbreaks of invasive aspergillosis among renal transplant recipients are very uncommon [3].

On February 6, 2001, the Infection Control Practitioner of a 350-bed acute-care hospital reported four invasive aspergillosis infections among renal transplant recipients during January-February 2001. Two cases had been reported in the previous two years, none among renal transplant recipients. Approximately 295 renal transplants are performed each year in this facility. To determine the extent of this outbreak and potential risk factors for invasive aspergillosis in the renal transplant population, an investigation was conducted that included cohort, environmental, and laboratory studies. Assistance with the investigation was provided by the Centers for Disease Control and Prevention (CDC), Division of Bacterial and Mycotic Diseases.

METHODS

Cohort Study: A retrospective cohort study was conducted among all renal transplant recipients who

* Adapted from Panackal AA, Dahlman A, Keil K, Peterson CL, et al. Outbreak of Invasive Aspergillosis among Renal Transplant Recipients. *Transplantation* 2002; (in press).

were hospitalized between January 1 and February 5, 2001 (study period). Medical records and radiographic, microbiologic, and pathologic reports were reviewed; information was collected about patient demographic and clinical characteristics, location during hospitalization, transplant characteristics, complications following transplantation, medications, laboratory findings, and outcome. A case of invasive aspergillosis was defined according to guidelines developed by the United States Mycoses Study Group and the invasive fungal infection group of the European Organization for Research and Treatment of Cancer [4]. In addition, descriptive data were collected on three case-patients that presented after the study period.

Environmental Study: In collaboration with the hospital and CDC engineers, an environmental examination of the hospital's facilities, focusing on areas of ongoing construction and where case-patients were hospitalized, was performed. The procedure manual for infection control during construction was reviewed, and the air filtration systems and water-damaged areas were inspected. The transplant pharmacist was interviewed regarding changes in the renal transplant immunosuppressive regimen usage, and the transplant surgeons, nurses, and operating room staff were questioned about changes in the patient care procedures and staffing.

Environmental surface samples were obtained from the areas of ongoing construction, renal transplant ward, operating room, intensive care unit (ICU) patient care areas, elevator, as well as heating, ventilation and air conditioning systems.

Laboratory Study: Identification of environmental and clinical isolates of *Aspergillus spp.* was performed by CDC. Molecular strain typing of isolates was performed by restriction fragment length polymorphism (RFLP) analysis.

RESULTS

Cohort Study: Forty renal transplant recipients were hospitalized during the study period; four cases of invasive aspergillosis were identified (attack rate = 10%). Three renal transplant recipients met the case definition of invasive aspergillosis with positive tissue histopathology and culture and one patient met the "probable" case definition based on clinical, radiographic, and culture criteria. *A. fumigatus* was isolated from all four case-patients. The median age of case-patients was 44 years (range 33-55 years). Three were male and three were Hispanic. The median time from last transplantation till diagnosis was 71.5 days (range: 58 to 415 days); all were admitted two or three times during the study period. Three presented with a clinical picture of pneumonia, and one was in congestive heart failure; all had evidence of renal dysfunction and received treatment for presumed organ rejection. All four case-patients died between 3 and 11 days after diagnostic culture collection.

Case-patients were significantly more likely to have received treatment for presumed organ rejection with sirolimus. Patients who received both sirolimus and mycophenolate -- simultaneously or sequentially -- were also at increased risk for invasive aspergillosis. Other factors found to be significantly associated with the development of invasive aspergillosis are highlighted in Table 1. The risk of disease associated with the use of mycophenolate and sirolimus during the study period persisted even after stratifying by prolonged corticosteroid use and certain induction agent usage (e.g. sirolimus).

There were no significant associations ($p>0.05$) between many other transplant-specific factors or host-related factors (Table 1). Environmental factors such as patient proximity to areas of construction and duration of hospital stay were also not found to be significantly associated with increased risk of invasive aspergillosis.

Three additional cases of invasive aspergillosis among renal transplant recipients occurred in the months following investigation (May to August 2001). These patients were designated as "OSP (outside study period) IA (invasive aspergillosis) patients 5, 6, and 7". OSP IA-patient 5 was on the renal transplant floor where construction continued after barriers were taken down. OSP IA-patients 5 and 7 received sirolimus

and mycophenolate; two OSP IA-patients died. In April 2001, at the conclusion of this investigation, CDC consultants recommended chemoprophylaxis using oral itraconazole solution for renal transplant recipients who were severely immunosuppressed. None of the OSP IA-patients received the recommended itraconazole prophylaxis.

Table 1. Risk factors for invasive aspergillosis among cohort of renal transplant recipients, January 1 - February 5, 2001.

Variable	Relative Risk	95% Confidence Interval	<i>P</i> value
Corticosteroids > 40 days (Prednisone \geq 20 mg)	29.8	4.0 - inf	<0.01
Pre-transplant hemodialysis > 40 years	21.0	22.5 - inf	0.01
Post-transplant hemodialysis > 7 days	11.0	1.4 - inf	0.02
Leukopenia (WBC <5,000/mm ³)	12.1	1.6 - inf	0.02
Sirolimus	17.7	2.3 - inf	0.01
Sirolimus + Mycophenolate	39.0	5.3 - inf	<0.01

Observational and Environmental Study: We observed that inadequate barriers, according to Hospital Infection Control Practice Advisory Committee (HICPAC) guidelines, were used between the construction site and the renal transplant ward [5]. In addition, considerable trafficking of staff between lockers within the construction area and patient care areas was occurring. Moreover, renal transplant patients had little or no respiratory protection when transported from their rooms off the floor, and patients shared the same elevators with construction workers and associated debris.

The ICU, where renal transplant recipients resided immediately post-transplant, was depressurized with air flowing into the patient area from the outside corridor. We observed water damage on the renal transplant ward ceiling tiles, ICU floor, and operating suite clean utility room.

The transplant team reported that immunosuppression regimens were altered, on an individual basis, by the transplant surgeon. The transplant pharmacists noted the use of sirolimus had increased five-fold in the two months prior to the outbreak. No other changes in patient care procedures and staffing were noted.

Laboratory Study: DNA fingerprinting analysis noted that only isolates from case-patients OSP IA-patients #5 and #6 had indistinguishable profiles; however, no genotype matches between environmental and clinical isolates were found.

DISCUSSION

This investigation suggests that renal transplant recipients can be at increased risk for invasive aspergillosis when highly immunosuppressed. The use of sirolimus with mycophenolate to treat transplant rejection, a regimen not approved by the Food and Drug Administration (FDA), demonstrated a strong association with invasive aspergillosis among renal transplant recipients. Such patients will benefit from application of established guidelines for prevention of invasive aspergillosis during construction activities in hospitals. Larger studies are needed to determine if the simultaneous or sequential use of sirolimus with mycophenolate has an independent role as a risk factor for invasive aspergillosis.

Because most of the case-patients were discharged and readmitted multiple times, exposure to *Aspergillus* in the community cannot be completely ruled out. Moreover, the incubation period for invasive aspergillosis is unknown, making it difficult to determine when exposure occurred [1]. However, the clustering of cases and the indistinguishable DNA fingerprints from two patients suggests transmission from a common source, likely the hospital. The lack of genotypic matches between environmental and clinical isolates is consistent with the knowledge that *A. fumigatus* has a very genetically diverse population [1].

We recommended environmental protective measures that follow the HICPAC guidelines, such as appropriate barrier placement, the use of high efficiency particulate air (HEPA) filter units, N95 respirator use by patients when traveling through potentially contaminated areas, preventing traffic between construction and patient-care areas, and designating one elevator for the exclusive use of construction workers and debris removal. Enhanced surveillance for invasive aspergillosis is ongoing at this facility.

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TYPE F BOTULISM DUE TO CLOSTRIDIUM BARATII

A 41-year-old woman, was transported by ambulance to the hospital on 29 January 2001 after awakening with shortness of breath and weakness. She complained of a one week history of upper respiratory infection, for which she had consulted her personal physician two days previously; she was prescribed amoxicillin. She said she had vomited several times that morning, and she felt dizzy with head movement. She had undergone a vaginal hysterectomy with anterior repair without complications at another institution 6 weeks previously for frequent bouts of cystitis. Past medical history also included a cholecystectomy and bilateral tubal ligation about 5 years previous.

A diagnosis of labyrinthitis was made and she was prepared for transfer to her usual hospital for further assessment. While lying on a gurney she suddenly became apneic with severe bradycardia. She was immediately resuscitated, intubated, and placed on mechanical ventilation and dopamine drip. She was obtunded but able to move her extremities in response to pain and verbal commands. All extremities showed weakness, and the pupils were dilated and slow to react to light; this was felt to be due to hypoxia during resuscitation.

She was admitted to the intensive care unit. Possible explanations for her collapse included intraabdominal bleeding related to her recent surgery, pulmonary embolus, or a central neurologic event. Ultrasonography and computerized tomography of the abdomen and pelvis showed a large ovarian cyst with no fluid in the pelvis or abdominal cavity. The pulmonary diffusion test showed normal circulation. Computerized tomography of the head was normal. The patient was unable to breathe on her own, and she continued to require dopamine to maintain perfusion.

A gynecology consultant saw the patient about 9 hours after the cardiac arrest. Bimanual pelvic exam confirmed an intact vaginal stump without discharge or bleeding, absence of uterus, and a left ovarian mass. Because of fever, an infectious disease consultant saw the patient about 24 hours after admission. Upon examination, all extremities moved in response to stimuli, and the pupils were reactive to light. Deep tendon reflexes were present and equal bilaterally. Examinations by a cardiologist and hematologist on the first hospital day also noted that the patient was moving all extremities, her pupils were dilated 4-5 mm and reacted slowly to light, and extraocular muscles were intact.

A neurology consultation was obtained about 30 hours after admission when nurses noted decreased voluntary movements. The patient was awake but unable to open her eyes. Strength in both hands and feet was normal, but there was no proximal movement and muscle tone was flaccid. Deep tendon reflexes and plantar reflexes were absent. Sensation appeared intact. Pupils were fixed and dilated to 7 mm, and extraocular movements were absent. She was able to squint her face and move the tongue slightly. Tomography of the head was normal. Spinal fluid had normal protein and glucose levels and was free of cells. The edrophonium test for myasthenia gravis was negative.

Over the next 12 hours the patient lost most voluntary muscle activity; she was only able to wiggle her toes bilaterally and move one finger. The diagnosis of botulism was considered and public health authorities were contacted to obtain botulinum antitoxin and arrange for diagnostic procedures. The patient received one unit of bivalent AB botulinum antitoxin 60 hours after admission. When preliminary toxin tests by the Los Angeles County Public Health Laboratory (PHL) suggested the presence of type E toxin in serum drawn prior to treatment, trivalent ABE antitoxin administered on the seventh hospital day.

Investigation for Botulinum Toxin and Toxigenic Clostridia

Clinical Specimens: A search was begun for possible contaminated food items or a potential wound as the source of her illness. Serum and stool specimens obtained prior to administration of antitoxin were tested by the PHL using the mouse bioassay. Type F toxin was detected in serum; this finding was confirmed by the California Microbial Diseases Laboratory. Sera taken on the fifth and ninth days after ad-

mission (three days after receipt of bivalent AB antitoxin and two days after receipt of trivalent ABE antitoxin, respectively) did not demonstrate the presence of botulinum toxin. Peritoneal fluid obtained by culdocentesis on the seventh hospital day was sterile and did not contain botulinum toxin.

Direct screening of the stool failed to demonstrate toxin. Cultures of stool did not identify organisms of *Clostridium botulinum*, nor was toxin demonstrated in the culture supernatant. Other organisms found in stool included *C. baratii*, *C. butyricum*, *C. perfringens*, *C. sordelii*, and other unidentified Gram-positive spore-forming rods, all of which were non-toxicogenic.

Potential Food Sources: The patient lived with her husband and two children, and her brother had been visiting prior to her illness. No other family members were ill, though they had eaten the same food for at least three days prior to her illness. Two days prior to admission the case prepared spaghetti and meat-based tomato sauce from a bottle. The only food consumed by the case but not by family members was canned tuna; the patient had opened and eaten two small cans of tuna with crackers and a commercial salsa about 18 hours prior to her first symptoms. There was no history of home-canned food items. On the third hospital day the family turned in a number of items taken from the garbage for possible testing.

- There were three tuna cans, two opened and one unopened. The two opened cans A & B appeared normal, without internal discoloration.
- Can A was relatively clean with flecks of tuna inside; rinse fluid was negative on direct toxin screening, and culture of the inside can wall found no clostridia.
- Can B contained semi-solid grease with bits of tuna, tomato meat sauce, and spaghetti. Direct toxin testing of the food mixture demonstrated type F botulinum toxin. Several bacteria were isolated, including *C. perfringens* and *C. baratii*; several of the *C. baratii* isolates produced type F toxin.
- Contents of a plastic storage bag with spaghetti, sauce, and meat were also cultured; toxigenic *C. baratii* that produced type F toxin was identified. Direct toxin testing was not performed.
- The unopened tuna can had the same lot number as the two that were consumed; it was released to the California Department of Health Services, Food & Drug Branch for examination. State investigators found no abnormalities in the can and the contents were sterile. The lot was traced back to a packing plant in Puerto Rico. Sterilization records were good, and few consumer complaints were on file against this lot.

Search for Wounds: Because of the history of recent gynecologic surgery, there was concern for a possible intra-abdominal or surgical wound abscess. The vaginal hysterectomy performed 6 weeks earlier was without complications, and recovery was uneventful. She had not complained of vaginal discharge after the immediate postoperative period, and had not resumed sexual relations with her husband. A follow-up examination 12 days prior to onset was normal. An ultrasound and computerized tomograph of the abdomen and pelvis on the day of admission detected a large left ovarian cyst but no free fluid in the peritoneal cavity. CT of the head was normal; MRI could not be performed because of cardiac instability. Another abdominal ultrasound on day 7 failed to show the ovarian cyst seen on admission, and considerable fluid was noted in the pelvis. A culdocentesis obtained clear fluid without cells or bacteria; aerobic and anaerobic cultures of the fluid were negative, as was direct botulinum toxin screening. Radiographs of the sinuses obtained on days 9 and 18 were normal. A full-body indium scan on the fifth hospital day was negative for any focus of inflammation; a repeat indium scan on day 18 for persistent fevers also yielded negative results. A lumbar puncture was repeated on the eleventh day; the protein level was normal and not elevated over the initial test on the day after admission.

CLINICAL COURSE

Renewed peripheral motor activity was noted on day 7 with return of distal, then proximal, upper and lower extremity movement. Deep tendon reflexes were normal by day 21. The patient was observed on day 30 performing her own suctioning and rolling in bed unassisted. Despite multiple attempts to wean off

the ventilator, she remained unable to sustain herself on room air. She was transferred after 7 weeks to a long term respiratory care facility, where she required mechanical ventilation for one more month.

DISCUSSION

The challenge was to determine if this was a case of classic foodborne botulism, intestinal botulism, or wound botulism. Points for and against each classification are shown in the table.

The patient apparently consumed a food item contaminated with toxigenic *C. baratii* and/or pre-formed toxin. The likely vehicle was spaghetti with meat sauce, prepared at home for the whole family 2 days before onset, and possibly eaten again by the case the following day without the knowledge of her family. Other members of the family may have reheated the food sufficiently to deactivate any toxin in their portions, or toxin may have been unevenly distributed. This toxigenic organism was found in two containers of food removed from the garbage (can B, sauce in plastic bag). From the available evidence it cannot be determined if the case consumed the toxin directly (foodborne botulism) or was colonized by a toxigenic clostridial organism (intestinal botulism). Lack of toxin in stool is not uncommon in confirmed foodborne botulism cases. In this case, the stool sample was small and hard, reducing the chances of finding toxin in detectable levels; a larger sample or enema fluid would have been preferred. Against the diagnosis of intestinal botulism is the presence of several non-toxigenic clostridial species in the stool despite ampicillin administered two days prior to admission; neither *C. botulinum* nor *C. baratii* was isolated.

The final impression was probable foodborne botulism, toxin type F.

<u>SUMMARY OF FINDINGS</u>		
	For	Against
Foodborne Botulism	<ul style="list-style-type: none"> • Initial presentation included vomiting. • Type F toxin was detected in direct test of mixed contents of a can removed from the garbage. • Type F toxigenic <i>C. baratii</i> was isolated from same can, as well as from a separate container of spaghetti sauce. 	<ul style="list-style-type: none"> • Toxin not detected in stool. • No one else in family was symptomatic. • There was no evidence to suspect the commercial tuna product.
Wound Botulism	<ul style="list-style-type: none"> • Recent (6 weeks) gynecologic surgery. 	<ul style="list-style-type: none"> • No focus of infection was identified despite extensive examinations and tests. • No signs or symptoms of post-operative infection (bleeding, discharge, dyspareunia) • Normal gynecologic examination 2 weeks PTA • Culdocentesis fluid tested negative for toxin.
Intestinal Botulism	<ul style="list-style-type: none"> • Possible altered gastrointestinal flora from antibiotic (ampicillin), analgesic (Vicodin), and/or antitomotility agent (oxybutynin). • GI tract abnormalities include status post cholecystectomy (5 years) and hiatal hernia. 	<ul style="list-style-type: none"> • Toxin not detected in stool. • Several clostridia were found in stool despite recent ampicillin administration for 1-2 days; none was toxigenic.

**PEDIATRIC HIV DISEASE:
 PEDIATRIC SPECTRUM OF DISEASE PROJECT**

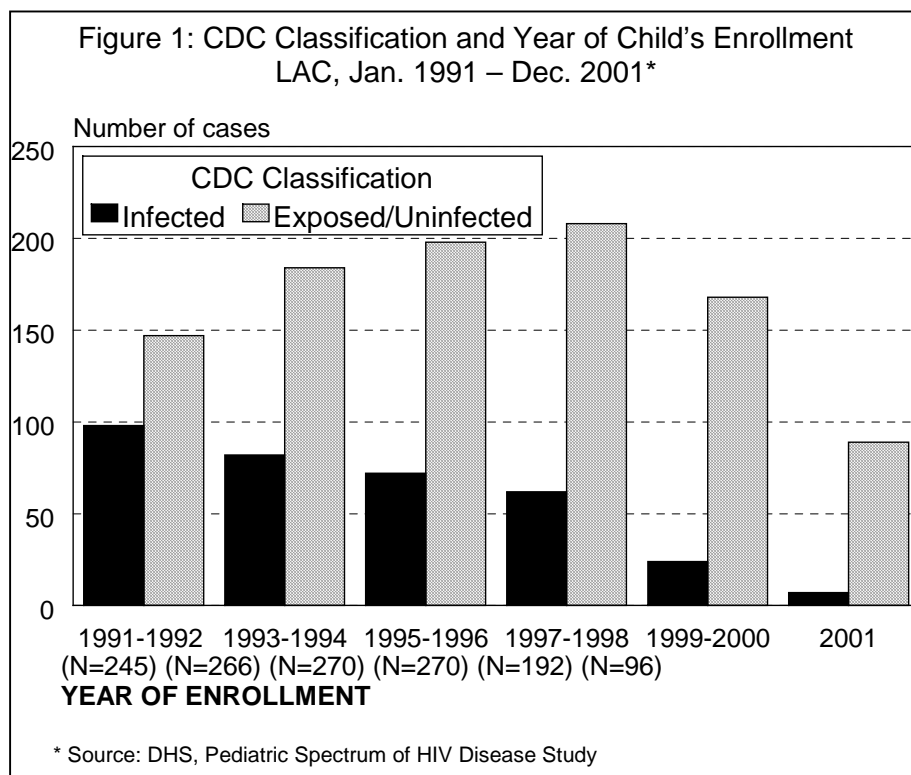
In March 1988, the Los Angeles County (LAC) Department of Health Services began conducting active surveillance for children HIV-exposed and infected under the age of 13 years as part of the Centers for Disease Control and Prevention's national Pediatric Spectrum of Disease (PSD) research project. Case ascertainment included all children who had died with an AIDS or HIV diagnosis and all who were still alive and under medical care. As of December 31, 2001, with active case surveillance at the 10 major LAC pediatric referral centers, a total of 1,746 HIV exposed and infected children have been reported to PSD (including those who had died). This number includes 1,531 LAC resident children and 215 nonresident children receiving care in LAC. PSD collects baseline information 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, 291 HIV-infected children and adolescents and 51 children of indeterminate status were under HIV care in LAC at the close of 2001.

CDC CLASSIFICATION

Of the total 1,746 children reported to PSD, 599 are HIV-infected, 1,032 are perinatally exposed but uninfected, and 115 are exposed and of indeterminate HIV status due to the persistence of maternal HIV antibody. Of the 599 HIV-infected children, 316 or 53% had an AIDS-defining condition and meet the CDC classification criteria for AIDS.* Of these, 27 were diagnosed with an AIDS defining illness after 12 years of age. An additional 26 infected children 13 years or older met the adult AIDS definition with a CD4 lymphocyte count <400 μ L. In 2001, 96 HIV-exposed or infected children were reported to PSD of whom 2 (2%) had an AIDS diagnosis at last medical contact, an additional 5 (5%) are infected but without AIDS, 40 (42%) are of indeterminate status, and 49 (51%) are uninfected. Of the 7 infected children reported in 2001, all were identified after birth. Two 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 11% in 2000-2001 (Figure 1).

MODE OF TRANSMISSION

Among the 714 HIV-infected children and adolescents, including 115 children with indetermi-



* Centers for Disease Control. Appendix: Revised Surveillance Case Definition for HIV Infection. MMWR Dec 10, 1999/4(RR-13);29-31.

nate HIV status, 536 (75%) had perinatally acquired (PA) infection from an HIV-infected mother, 126 children (18%) were infected from a contaminated blood transfusion, and 39 (5%) were children with hemophilia or a coagulation disorder. Two children were infected due to breast feeding. Among the PA group, 22% had a mother who was an intravenous drug user (IDU), 12% 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.

The proportion of perinatally exposed children whose mother's risk factor for HIV was IDU has decreased from 37% in 1988-91 to 7% in 2001 (Figure 2). Correspondingly, the number of children infected by to an HIV-infected mother with unknown risk has increased each year from 24% in 1988-90, to 55% in 1997-1998, and 46% in 2001. The proportion due to known heterosexual contact has increased since 1997-98 from 25% to 42% in 2001.

DEMOGRAPHICS

Among the 714 HIV-infected and indeterminate children reported, 34% were Black, 43% Hispanic, 20% White, 3% Asian, and 1% other/unknown. Of the 96 HIV-exposed and infected children reported in 2001, 33% were Black, 56% Hispanic, and 9% White.

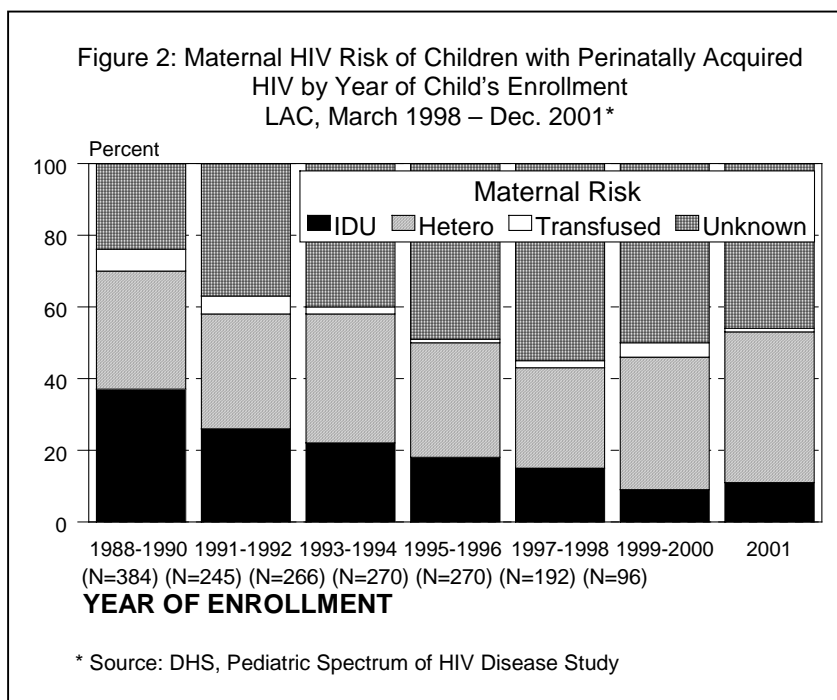
The gender distribution of HIV-infected and indeterminate children shows slightly more males than females (52% vs. 48%) due to the disproportionate number of transfusion-associated and hemophiliac cases among males.

Most children (73%) had a biologic parent as their primary caretaker at the latest medical contact; 19% lived with another relative or were in foster care, 4% 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 transfused cases and hemophiliacs (24% vs. 4% and 3%, respectively). Within the PA group, Hispanics were the least likely to be in foster care or living with another relative (14% vs. 32% for Blacks and 29% for Whites).

CASE FATALITY AND SURVIVAL

The cumulative fatality rate for AIDS cases was 64% (198/309). Fifteen (4%) of the children not meeting the AIDS case definition have died. The mean age at AIDS diagnosis for the PA cases was 30 months (median 15.0 months) compared to the mean age at AIDS diagnosis of 90 months for transfused cases (median 89 months), and 160 months for hemophiliacs (median 143 months).

Among the 342 HIV-infected and indeterminate children still alive and followed by PSD, 17% were less than 2 years of age, 24% were between 2-7 years, 31% were 8-12 years, and 28% were 13 years or greater.



PRENATAL PROPHYLAXIS AND PERINATAL TRANSMISSION

Beginning in 1994, zidovudine (ZDV) administered during pregnancy, labor and delivery, and to the newborn became a recognized means to prevent perinatal HIV transmission. Of the 729 infants born in 1995-2001 to HIV-infected women and reported to PSD, 534 (73%) of their mothers received ZDV during pregnancy; 82% received prenatal care. Similarly, 556 (76%) received ZDV during labor and delivery. In 2001, 89% received prenatal care, 90% received antiretroviral therapy 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 1995-01 and reported to PSD was 9%. The C-section delivery rate reported to PSD has increased from 20-30% before 1999 to 57% in 2001.

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 80% acceptance rate for 2001. No HIV-positive women were identified in 2001. 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.

**LATE SEASON LIGHT SEASON:
LOS ANGELES COUNTY INFLUENZA SURVEILLANCE AND
ELEMENTARY SCHOOL OUTBREAKS, 2001-2002**

In Los Angeles County (LAC), as in other areas across the US, influenza surveillance presents a unique challenge since most people affected by the disease do not seek medical care, and even if they did, individual cases are not reportable or counted by health departments. Tracking individual cases would overwhelm any health department because so many people are susceptible and infected yearly; during a mild season it is estimated about 10% to 15% of the population becomes infected; in a more severe season, 20% or more of the population can suffer from influenza. In light of the high morbidity and mortality due to influenza, the impact it can have on our health system, and the need to identify new strains of the ever-changing virus, influenza surveillance remains an important public health responsibility.

ACDC employs a variety of strategies to determine the seasonal impact of influenza in LAC. These methods can be classified under three major categories of surveillance: 1) direct methods which include tracking viral isolates and investigating community outbreaks, 2) indirect methods which monitor the secondary consequences of influenza (e.g., pneumococcal and influenza mortality rates), and 3) comparisons to state-wide and national findings.

The following summarizes the major events which occurred during the 2001-2002 influenza season as well as surveillance efforts which detail the seasons' occurrence and impact of influenza.

EVENT SUMMARY

There were several events that potentially influenced the onset, acceleration and duration of influenza during the 2001-2002 season. First, similar to the previous season, the 2001-2002 season began with a delay in vaccine distribution and an initial shortage of supply. However, the previous season (2000-2001) was fraught with problems associated with vaccine shortages and delays (i.e., clinics were deluged with patients requesting vaccinations causing session cancellations due to exhausted supplies, and ultimately, the shortage lasted well into the season). In sharp contrast, during fall of 2001, the shortages and delays were not as severe, plus methods for staggering vaccine distribution were well publicized allowing high-risk individuals first priority. As a result, during 2001-2002, there were no major problems immunizing county residents.

The two most significant characteristics of the 2001-2002 season were how mild it turned out to be (as illustrated by the comparison of viral isolates below), and how long it lingered beyond a typical season, culminating with a surge in type B infections during late March (described in the elementary school outbreaks below). While it is impossible to pinpoint a definitive cause to account for the season's dramatic decrease in severity, there are several potential contributing factors:

1. An unexpected consequence of the September 11 terrorist attacks and anthrax scare:
There are several reasons why the terrorist attacks and anthrax scare may have contributed to a reduction in the incidence of influenza during the 2001-2002 season. First, the plane hijackings led to dramatic restrictions in travel – numerous flights were canceled and trips were postponed. Thus while, early in the season, there were pockets of high influenza activity across the US, infection did not successfully spread beyond those areas. But more than canceled travel, during Fall 2001, one can speculate that people weren't socializing in general – attending parties and going out seemed inappropriate following the attacks; many events were canceled and stores and other venues reported significant drops in attendance. This, again, likely limited the spread of influenza infection. Finally, although largely anecdotal, the anthrax scares may have prompted the public to be more conscientious about good hygiene and health habits (e.g., washing hands, covering mouth when coughing/sneezing, etc.).

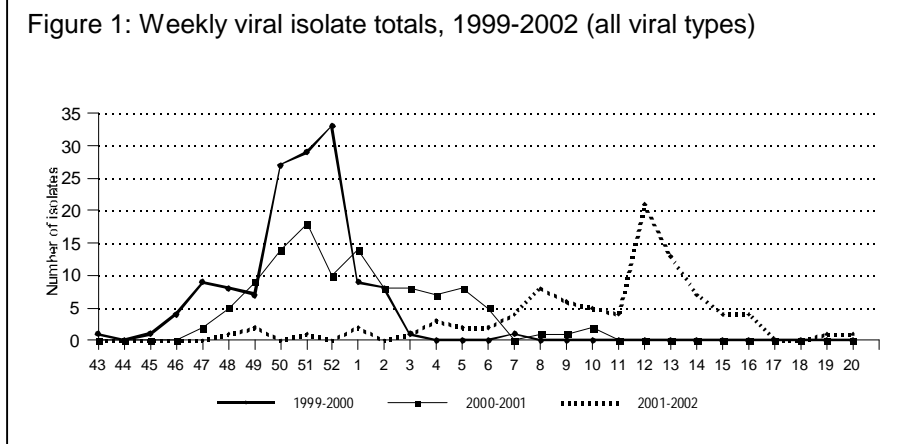
2. Similar Type A viral strains in circulation:

Another reason for the mild influenza season can be linked to the type of viral strains that have been in circulation. Aside from a novel type B strain that emerged late in the season (which caused widespread elementary school outbreaks described below), the type A strains have been fairly consistent over the past few years. Thus, it is likely that much of the public have already developed immunity, either naturally through past exposure, or by vaccination, which closely matched the strains that circulated during 2001-2002.

VIRAL ISOLATE COLLECTION -- LATE SEASON, LIGHT SEASON

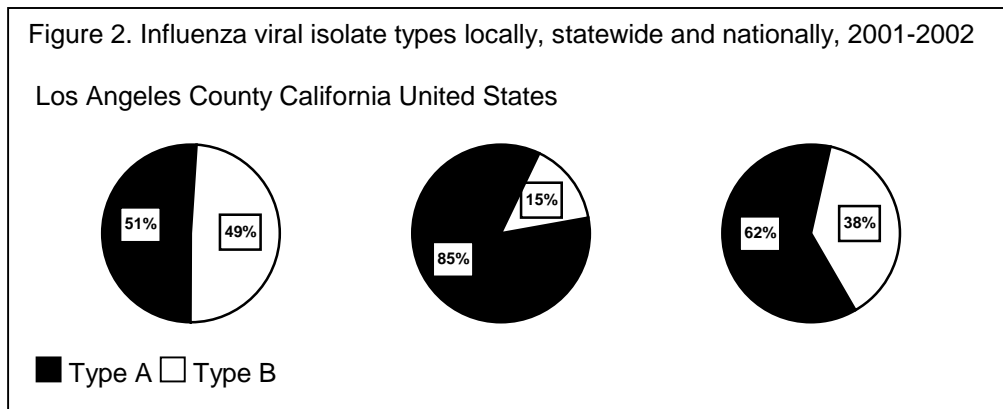
In order to assess the seasonal pattern of influenza activity in LAC, during the winter months, influenza viral isolates are reported weekly to ACDC from Kaiser Permanente, Children’s Hospital and Cedars Sinai laboratories. When combined with clinical information from the community, these isolate reports 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.

Comparing the weekly total number of influenza viral isolates reported over the past three seasons, the differences are evident (Figure 1). 2001-2002 was clearly a late season – the first reported case did not occur until early December, nearly two months later than the previous two seasons. In addition, during 2001-2002, there was no substantial peak in isolates



around the new year (late December to early January), when influenza typically increases in LAC. Instead, activity peaked during late March (weeks 12-13), and this increase was due entirely to outbreaks of type B influenza. Overall, 2001-2002 was also a light season; there were 20% fewer isolates than reported in 2000-2001, and 35% fewer than reported in 1999-2000.

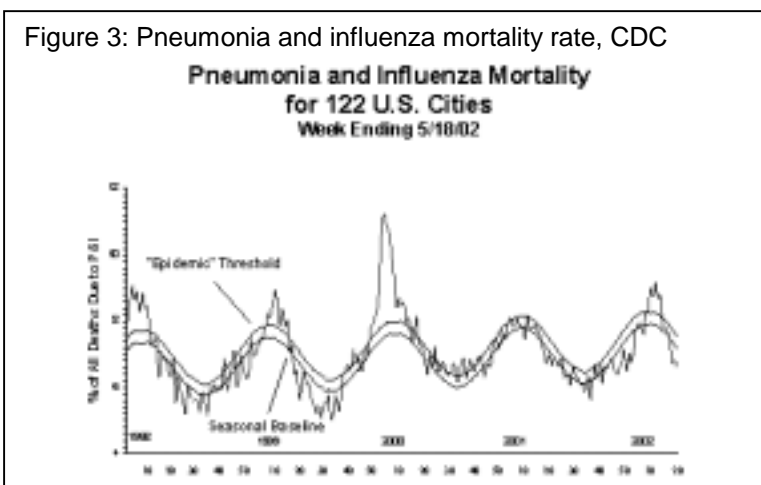
Another distinguishing feature of the 2001-2002 season was the high proportion of type B influenza activity nationally and especially locally (Figure 2). During the 2001-2002 season, nearly half of the isolates reported to ACDC were type B (49%), across California, 15% of the reported isolates were type B, and nationally, more than a third of the isolates (38%) were type B. During the previous season (2000-2001),



an even greater proportion of the isolates were identified as type B – 58% identified from LAC surveillance, 38% from the California state-wide surveillance and 27% from the national surveillance.

INFLUENZA/PNEUMONIA MORTALITY

The national pneumonia and influenza (P&I) mortality statistics also reflect how mild the 2001-2002 influenza season was (Figure 3); while there was a minor increase in the death rate during February 2002, this increase is clearly much less pronounced than what occurred during the 1999-2000 season. Last season, 2000-2001, the national (P&I) mortality rate was even smaller; the number of deaths reported never exceeded the epidemic threshold.



ELEMENTARY SCHOOL OUTBREAKS (LATE SEASON, TYPE B)

Long after influenza activity was expected to conclude for 2001-2002, LAC experienced a late-season surge of type B influenza which began in mid-March and extended into April. This illness primarily affected elementary and middle school children and accounted for substantial rates of school absenteeism, as high as 15-20%. Outbreak investigations were conducted at a total of 6 schools across LAC (1 middle school and 5 elementary schools). While it was especially unusual for influenza to occur so late in the season, cultures collected from students and faculty at four separate schools confirmed the presence of influenza type B (Table 1); of the 16 cultures collected, 9 (56%) tested positive, all for influenza type B.

Table 1: Summary of investigated school outbreaks, 2002

School	Zip Code	Collection date	Number of Specimens collected	Number (%) of positive specimens*
School A	90032	3/22	2	1 (50%)
School B	90278	3/28	5	5 (100%)
School C	91770	3/28	5	2 (40%)
School D	90037	4/4	4	1 (25%)
School E	91780	--	0	--
School F	91733	--	0	--
total			16	9 (56%)

* All cultures were positive for influenza type B.

There were several notable features of this late-season peak in activity. First, the symptoms were not always classic for influenza (Table 2). The primary common symptoms were fever (101⁰-103⁰), headache, sore throat, cough and fatigue; however, symptoms in some cases also included runny nose and congestion. Second, as noted above, illness predominantly affected elementary and middle school children.

Some school nurses, who normally send home only a few ill children per week, reported sending home as many as 39 ill children in one day. In addition, activity was very widespread, reaching across all corners of the county and as far south as Orange County. Moreover, while the illness appeared to mostly effect school-aged children, illness often extended throughout their households; in a small survey of symptomatic children (n=51), nearly half reported other family members also ill (Table 2). Nonetheless, the illness itself was short-lived with a duration of approximately 4 days – thus while this illness had an intense immediate impact, the extent of illness subsided quickly. It appears that spring break vacation inhibited its continued spread.

Perhaps the most significant factor of these outbreaks was the type of strain identified. Additional typing conducted by the California state laboratory identified the virus as a novel strain previously limited to Southeast Asia (B/Hong Kong/330/2001). The majority of B isolates worldwide during the 2001-2002 season were characterized as another strain (B/Sichuan/379/99). Moreover, the novel B strain which caused the late season outbreak in LAC was not included in the 2001-2002 vaccine, and the strain included was incapable of providing sufficient immunity to this new strain.

Table 2: Summary of symptoms

Symptom	School A (n=15)	School B (n=7)	School C (n=25)	School D (n=4)	Overall (n=51)	%
Fever	13	4	22	4	43	(91%)
Tired/fatigue	15	4	15	3	37	(79%)
Headache	10	5	19	1	35	(74%)
Runny nose	3	6	20	4	33	(70%)
Weakness	10	6	14	2	32	(68%)
Cough	6	6	18	0	30	(64%)
Congestion	8	4	12	3	27	(57%)
Sore throat	5	6	15	0	26	(55%)
Body ache	2	5	13	2	22	(47%)
Chills	2	6	10	3	21	(45%)
Abdominal cramps	2	1	8	3	14	(30%)
Nausea	1	2	10	0	13	(28%)
Ear pain	0	2	9	2	13	(28%)
Vomiting	0	2	9	1	12	(26%)
Diarrhea	1	1	3	1	6	(13%)
Rash	0	0	3	0	3	(6%)
Other in family sick?	5	0	15	3	23	(49%)

Important vaccination changes. The late season outbreak investigations in LAC contributed to two very important changes for the upcoming 2002-2003 influenza season. First, in order to offer immunity to the novel B strain, B/Hong Kong/330/2001 will be added to the 2002-2003 vaccine. Second, since this strain

accounted for substantial (and unexpected) rates of morbidity and mortality among the very young, the Advisory Committee on Immunization Practices has modified their vaccination recommendations. Starting in the Fall of 2002, children between the ages 6 months to 23 months will now be classified as “high-risk,” thereby warranting early immunization against influenza.

CONCLUSION

The 2002-2003 season illustrates several important factors regarding influenza.

1. Influenza is very unpredictable.

While numerous years of surveillance have identified some common influenza trends (i.e., the general time of onset and peak), these trends are not absolute – core aspects can change in a given year, often surprising even the most seasoned influenza investigators. In LAC, the 2002-2003 season was especially unpredictable; not only was activity much milder than previous years, activity began much later than expected, it did not peak during the usual time and it continued well beyond an ordinary season.

2. Influenza can extend into the Spring.

One unpredictable aspect of influenza is its duration. As the 2002-2003 season demonstrated, influenza activity can extend into the Spring. Consequently, clinicians should not discount influenza as a potential diagnosis simply because the season has changed.

3. The type of strain is important.

Influenza is often discussed as if it is a disease with a single underlying cause, but as the 2002-2003 season demonstrated, that is certainly not the case and identifying the type of viral strain is critical for several reasons. First, some testing methods as well as some medications used for treatment and prophylaxis are designed solely for type A influenza. And while type A is frequently the more common circulating strain, occasionally type B strains predominate – as was the case during the last two seasons in LAC. Moreover, characterizing the virus is critical in order to distinguish novel strains and to perfect the vaccine. The high incidence of infection which occurred during March 2002 can be traced back to the fact that the strain was new and immunity (either through natural exposure or through vaccination) was not possible. ACDC’s surveillance added to the body of knowledge that was used to modify the vaccine as well as to change the policy for immunization priority for the following year. These changes will likely decrease subsequent morbidity and mortality due to influenza.

OUTBREAK OF GASTROINTESTINAL LISTERIOSIS ASSOCIATED WITH CONTAMINATED DELI MEAT*

The Los Angeles County Department of Health Services (DHS) received a report of a diarrheal illness cluster on June 6, 2001 associated with a birthday party catered by a local delicatessen three days earlier. Approximately 60 individuals attended the party and 28 reported illness. Because of the temporal association of the symptoms with the party and the involvement of a commercial establishment, DHS investigated.

Listeria monocytogenes (LM) causes an estimated 2,500 serious illnesses and 500 deaths per year in the US [1]. It most commonly presents as severe systemic illness (sepsis, meningitis, encephalitis) in persons with impaired cell-mediated immunity – such as infants, the elderly, the immunocompromised, and pregnant women [2]. Foods found to be associated with LM include soft cheese, raw milk, hot dogs, deli meats, seafood, and fresh vegetables [3]. A less common foodborne febrile gastrointestinal syndrome has been described in healthy persons, with onset of fever, muscle aches, headache, and diarrhea, 9-48 hours after exposure [4,5].

METHODS

ACDC conducted a cohort investigation of party attendees, using a telephone questionnaire. Delicatessen employees were also interviewed. Case finding consisted of contacting other at-risk customers and events identified from delicatessen invoices from May 15 to June 7. Identified customers were contacted by facsimile or by mail with telephone follow-up. Enhanced surveillance for listeriosis was also done, with alerts being sent to district public health nurses and hospital infection control practitioners.

A *presumptive case* was defined as any birthday party attendee with at least one systemic symptom (e.g., fever, body aches, or headache) and at least one gastrointestinal symptom (e.g., diarrhea, vomiting, cramps, or nausea). A *suspect case* was defined as above, but in any other – that is, non-birthday party – customer of the delicatessen during the study period. A *confirmed case* was any birthday party attendee, or other customer of the delicatessen during the study period, who had a blood or stool culture that was positive for the outbreak strain of LM.

Stool and leftover food specimens were requested from all ill party attendees and delicatessen employees. EHS inspected the delicatessen kitchen facility on multiple occasions. Environmental swabs of the kitchen were obtained for culture. PHL tested stool specimens for *Salmonella*, *Shigella*, *Campylobacter*, *E. coli* 0157-H7, and *Yersinia enterocolitica*.

RESULTS

Of an estimated 60 individuals attending the party, 44 were interviewed (response rate 73%). Of 44 interviewed reported illness, 16 met the definition for a presumptive case (attack rate 36%). Three six-foot submarine sandwiches were ordered and made the same day as the party: Sandwich A consisted of half turkey and half vegetarian, with pepper jack cheese throughout; Sandwich B consisted of turkey and cheddar cheese throughout; and Sandwich C was half roast beef and half ham, with Swiss cheese throughout. Other food items included potato salad, ice, store-bought taquitos, watermelon, guacamole, chips and soft drinks; strawberries from a local farm; cake from a bakery; and a home prepared onion dip.

Case characteristics: The median age of presumptive and confirmed cases from the birthday party cohort was 15.5 years (range 7-66 years); half were male. The mean incubation period was 21 hours (range 6-

* Authors for this submission include: Douglas M. Frye, M.D., M.P.H. of the HIV Epidemiology Program, Rachael Zweig, M.P.H., Irene Lee, M.P.H., Michael Tormey, M.P.H., and Laurene Mascola, M.D., M.P.H., of Acute Communicable Disease Control; Joan Sturgeon, B.S. of the Public Health Laboratory; and Michelle LeCavalier, M.S., R.E.H.S. of Environmental Health Services.

35 hours). Symptoms included: body aches, 14 (93%); fever, 13 (81%); headache, 13 (81%); diarrhea, 10 (63%); and vomiting, 9 (56%).

Food-specific analysis: All 16 reported cases had eaten turkey, 15 from Sandwich A and 1 from Sandwich B. Both sandwiches were made from the same previously unopened package of whole, unsliced turkey breast. Eating from Sandwich A was significantly associated with illness (Relative Risk [RR]=5.6; $p < 0.002$), while eating from either Sandwich B (RR=0.1; $p < 0.01$) or Sandwich C (RR=0.2; $p < 0.01$) was protective. Consumption of turkey and pepper jack cheese were associated with illness on univariate analysis (Table 1). Turkey consumption could account for 100% of cases, while pepper jack cheese could only account for 56%. Upon stratified analysis, only consumption of turkey remained significant ($p = 0.003$). Furthermore, neither of the 2 persons who ate only the vegetarian portion of Sandwich A, which also contained pepper jack cheese, became ill. No other food items were associated with illness.

Table 1. Univariate analysis of potential food vehicles for outbreak of *L. monocytogenes*-associated gastroenteritis among attendees of a catered birthday party.

Food Item	Number (Attack Rate %)		Rate Ratio	95% CI	p value
	Case (n=16)	Non-ill (n=27)			
Turkey	16/6 (100)	6/24 (25)	undefined	undefined	0.000004*
Lettuce	11/16 (69)	9/18 (50)	1.5	0.7, 3.5	0.3
Cake	10/16 (63)	18/25 (72)	0.8	0.4, 1.7	0.5
Taquitos	9/16 (56)	12/25 (48)	1.2	0.6, 2.7	0.6
Tortilla chips	9/16 (56)	12/21 (57)	1.4	0.5, 3.6	0.7
Pepper jack cheese	9/16 (56)	13/22 (59)	undefined	Undefined	0.004**
Chips	8/16 (50)	14/25 (56)	0.9	0.4, 1.9	0.7
Tomato	8/16 (50)	9/18 (50)	1.0	0.5, 2.0	1.0

* When stratified by pepper jack cheese, turkey remains significantly associated with illness ($p = 0.003$).

** When stratified by turkey, pepper jack cheese is no longer significantly associated with illness ($p = 0.1$).

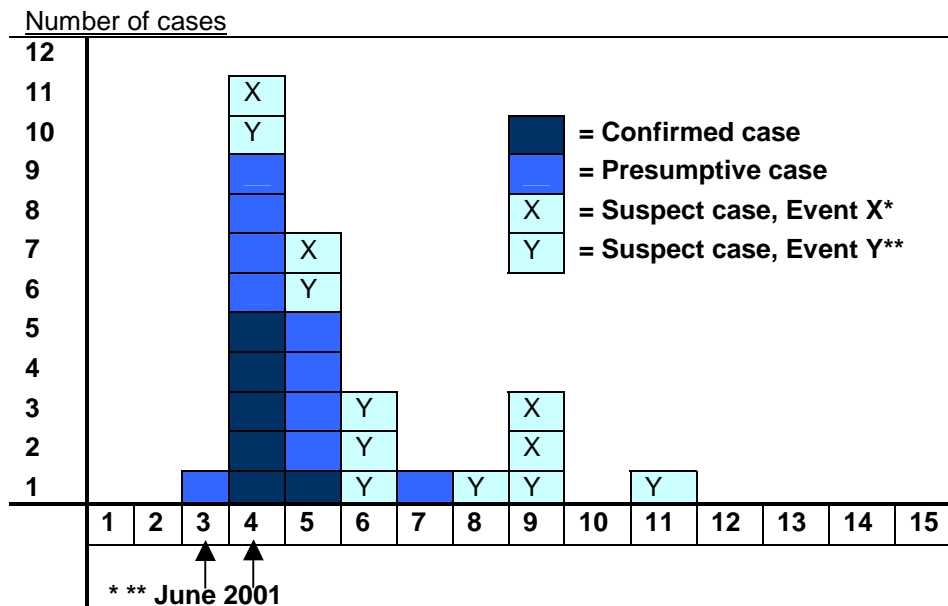
Stool Testing: Initial stool cultures on 6 cases were negative for routine enteric pathogens (*Salmonella*, *Shigella*, and *Campylobacter*), *Yersinia enterocolitica* and *E. coli* O157:H7. Isolates from 6 cases were confirmed as LM and shared an indistinguishable PFGE pattern.

Case finding: Delicatessen invoices from May 15 to June 7, 2001 were reviewed and 60 additional events were identified who had ordered suspect foods from the delicatessen. Each identified party was contacted and asked about illness. Clusters of suspect cases were found in two unrelated events, X and Y (see Figure 1). Five of the 8 cases from Event X had eaten food from the delicatessen on the same day as the birthday party. Four of the 5 cases, but only 2 of 16 non-ill persons, reported having eaten turkey on that day (RR=10; Fisher exact $p = 0.01$). Stool cultures from 5 suspect cases were negative for LM. Six of 8 suspect cases from Event Y had eaten food from the delicatessen made from the same package of turkey implicated in the outbreak. Five of these 6 cases, but only 9 of 27 non-ill persons, in Party X reported having eaten turkey from the delicatessen on that day (RR=6.8; Fisher exact $p = 0.06$). Stool cultures from 4 suspect cases were negative for LM. Heightened surveillance for listeriosis in the ensuing months failed to identify any cases linked to this outbreak or matching the outbreak strain.

Retail Food Establishment Inspection: Investigation of the delicatessen's kitchen revealed multiple health code violations, including a general lack of cleanliness, inadequate sanitization, and a large walk-in refrigerator at a temperature of 51-54°F (11-12°C). Of the 30 environmental swabs taken from the delicatessen's kitchen and walk-in refrigerator, after the delicatessen had been thoroughly cleaned, all tested

negative for LM. None of the 9 employees who completed questionnaires reported illness. Stool specimens from the 2 of 7 employees who provided them tested negative for LM, including the sandwich maker.

Figure 1. Epidemic curve of presumptive and confirmed cases for an outbreak of *L. monocytogenes*-associated gastroenteritis among attendees of a catered birthday party, including suspect cases from two unrelated events using the same caterer on June 3 and 4, 2001.



* The birthday party and Event X served food from the delicatessen on the same day, June 3; the onset date was unknown for 1 of 5 Event X cases and is not included here.

** Event Y served food from the delicatessen on June 4 that included turkey from the same package implicated in the birthday party outbreak.

Food Sample Testing: Four samples of home-refrigerated leftover portions of Sandwich A (including one sample of turkey and one of pepper jack cheese) were all negative for *Salmonella*, but grew the outbreak strain of LM. Quantitative testing performed on a 1-gram sample of turkey taken from the leftover sandwich yielded LM at 1.6×10^9 CFU/gram. Previously unopened packages of pepper jack cheese and turkey breast obtained from the delicatessen tested negative.

Trace back: We identified the out-of-state plant that processed the turkey breast, but an investigation of that plant was not done. The United States Food and Drug Administration did investigate processing plants that produced and distributed the pepper jack cheese, finding no health code violations and taking no food or environmental samples for testing.

DISCUSSION

An outbreak of febrile gastroenteritis due to LM occurred among healthy attendees of a catered birthday party who consumed highly contaminated delicatessen meat. Systemic symptoms were prominent among cases, but no invasive disease was identified. LM is a slow-growing organism under the most favorable of conditions and febrile gastrointestinal illness in healthy persons has been seen when contamination of a

ready-to-eat food item is followed by prolonged holding of that food out of temperature[4,5]. We hypothesized the source of contamination of this outbreak to be a single package of processed turkey breast held for an indeterminate number of days in a delicatessen walk-in refrigerator that was found to be out-of-temperature upon inspection. While we traced the implicated food source to an out-of-state meat-processing plant, an investigation of that plant was felt to be unfeasible, due both to the absence of a lot numbers for the implicated package of turkey breast and to the apparently limited nature of the outbreak.

Extensive case-finding efforts looking at other events who patronized this delicatessen during a 3-week period revealed two clusters of persons ill with symptoms of febrile gastroenteritis. Nevertheless, letters were sent out to all those potentially exposed to LM, instructing high-risk individuals to contact their doctor if they experienced a febrile illness in the next 2-6 weeks.

RECOMMENDATIONS

Clinicians and health officers should think of LM when signs and symptoms are consistent with the diagnosis and routine enteric cultures are negative.¹ Especially in an outbreak of febrile diarrhea, clinicians and health officers should ask the laboratory to hold stool specimens of presumptive cases until results of enteric cultures are known, so that further testing for LM. Clinicians should also counsel their high-risk patients to avoid soft cheeses and deli counter food, and to cook leftover food and ready-to-eat foods until steaming hot [3,6].

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MYCOBACTERIUM FORTUITUM COLONIZATION IN A HOSPITAL TUBERCULOSIS UNIT

This report summarizes an investigation of a cluster of patients with *Mycobacterium fortuitum* respiratory tract colonization in a tuberculosis unit at a hospital. This opportunistic organism commonly uses water as a vehicle for infecting or colonizing humans. Although all the patients were colonized in their sputum, the investigation ensued because of the potential threat of infection in this immune compromised group. The focus of this investigation was to verify the increase of *M. fortuitum* in the hospital by reviewing laboratory data and to identify possible environmental sources of contamination.

BACKGROUND

Hospital X is a 170-bed facility located in Service Planning Area 1 (SPA 1). The hospital provides acute medical, surgical, comprehensive acute medical rehabilitation and extended skilled nursing services. Recalcitrant TB patients are sent to the skilled nursing facility TB unit (SNFTB) from all parts of the State. The facility has approximately 1,400 admissions and 59,000 outpatient visits per year.

In the fall of 2000, DHS TB Control Program noted an increase of respiratory tract *M. fortuitum* isolates from Hospital X. The hospital was notified and conducted its own investigation with assistance from the SPA 1 Medical Director by reviewing laboratory data, patient clinical data, and infection control procedures. They also consulted the LAC Public Health Laboratory (PHL) that processes all Hospital X's clinical specimens for acid-fast bacilli (AFB). Despite implementing control measures, patients continued to become positive for *M. fortuitum*. On February 15, 2001, Acute Communicable Disease Control Unit (ACDC) was contacted to assist with the investigation and to provide guidance in collecting environmental specimens.

METHODS

Case Ascertainment and Background Statistics. A case-patient was defined as a SNFTB unit inpatient from Hospital X with an AFB culture positive for *M. fortuitum* between July 1999 and January 2001.

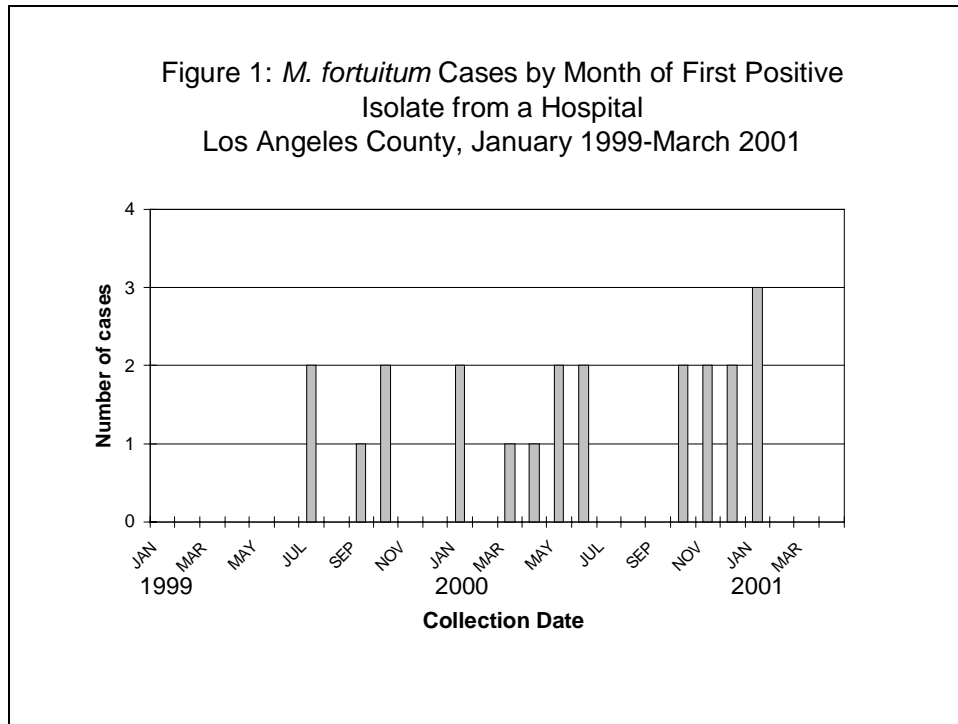
The infection control practitioner (ICP) provided ACDC with information from chart reviews of 20 patients with *M. fortuitum* from July 1999 to January 2001. Information about the layout of the Hospital X and its water reservoir system was obtained. To confirm the increase of cases and to find additional cases, the PHL provided AFB laboratory results for *M. fortuitum* at the facility and other LAC health facilities from January 1998 to March 2001. Two additional cases were identified from the PHL records.

Environmental Laboratory Investigation. On March 20, 2001, ACDC collected 22 environmental specimens throughout Hospital X. From information provided by the ICP and based on the current literature [1], ACDC was able to determine possible environmental sources where cases might have been exposed. Specimens were collected from the SNFTB Unit and other areas around the hospital, including ice and water from ice machines, a water filter cartridge, drinking fountains, showers, sinks, and outside reservoirs. Specimens were submitted to the PHL for isolation and identification.

RESULTS

Case-Patients. Twenty-two case-patients were identified from July 1999 to January 2001 (Figure 1). They all had *M. fortuitum* isolated from sputum cultures submitted for AFB testing. Of the 20 cases where complete laboratory information was available, 16 (80%) had smear negative AFB results and 4 (20%) had rare to moderate growth. Case-patients averaged 50 years old with a range from 32 to 83 years. All were male except one. Only one had HIV infection. All cases were admitted to the SNFTB unit at least two days before being identified culture positive for *M. fortuitum*. No other patients in other parts of Hospital X

were identified with this organism. Assuming that exposure was from unit admission date to date of first positive culture, cases were exposed to the SNFTB unit for an average of 33 days (range= 2 to 103 days) before being colonized. Nineteen cases had a primary diagnosis that included pulmonary TB. Other diagnoses included miliary TB, laryngeal TB, meningeal TB, genitourinary TB, hepatitis C, diabetes I and II, chronic renal failure, and hyperparathyroidism. There were no changes in patient census, laboratory methods or other apparent explanations for the increase of cases.



Analysis of Background Statistics. From information provided by the PHL, Hospital X did not have a high proportion of *M. fortuitum* isolates (0.2%) from submitted AFB specimens compared to the other DHS hospitals and to the overall incidence for all LAC health facilities (0.5%) for the comparison period January 1998 to June 1999 (Table 1).

Table 1: *Mycobacterium fortuitum* Isolates Identified by the Public Health Laboratory, January 1998 – June 1999 and August 2000 – November 2000

Health Facility*	Jan 1998 – June 1999			Aug 2000 – Nov 2000		
	Number**	(%)	Total AFB	Number***	(%)	Total AFB
Hospital X	2	(0.2)	829	5	(2.0)	256
Hospital A	4	(0.5)	752	0	(0)	418
Hospital B	1	(0.8)	120	1	(0.2)	468
Hospital C	5	(0.2)	3334	6	(0.9)	683
Hospital D	1	(0.2)	425			
Clinic X	7	(1.5)	470	3	(2.3)	130
All other facilities	117	(0.5)	21665			
Total	137	(0.5)	27705			

*Hospitals A-D, Hospital X, and Clinic X are DHS facilities.
 **Date of collection.
 ***Date of specimen received in Public Health Laboratory. May vary a few days from date of collection.

In addition, data for isolates from DHS hospitals and a nearby Clinic X during the peak of the cluster (August to November 2000) were examined (Table 1). Aside from the Clinic X, which is in the same geographical area, Hospital X had the highest proportion of *M. fortuitum* isolates identified compared to the other DHS hospitals. It is also interesting to note that Clinic X was high for both time periods (1.5% in January 1998-June 1999 and 2.3% in August-November 2000).

Examining Table 1, there was as a 9-fold increase of the proportion of *M. fortuitum* isolates from Hospital X (2.0%) during the peak compared to the rate (0.2%) for the comparison period.

Environmental Laboratory Investigation. All environmental cultures of specimens taken from Hospital X were negative for *M. fortuitum* and other mycobacterium species.

DISCUSSION/CONCLUSIONS

Twenty-two patients were identified with *M. fortuitum* respiratory tract colonization from July 1999 to January 2001 after being admitted to the SNFTB unit at Hospital X. Cases peaked in January 2001 and ceased in February 2001. There was a documented increase of cases during this period compared to the previous year and a half and that increase was higher than what was occurring in other DHS hospitals.

This investigation did not determine the source for the increase of cases. The medical literature would suggest that water was the most likely source, although this was not confirmed by this investigation since all environmental cultures taken were negative for *M. fortuitum* and other mycobacterium species. Our investigation does not rule out the presence of the organism during the time of the increase, since our specimens were collected two months after the last case was detected. At the time of collection, contamination may have been transient but this is unlikely since cases have ceased to occur at the facility.

Since rapidly growing mycobacteria like *M. fortuitum* are readily recovered from soil, dust, and water, continued surveillance and strict adherence to infection control procedures, particularly for immune compromised individuals, are necessary to prevent colonization and potential morbidity by this organism.

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COMPLETENESS OF HOSPITAL PERTUSSIS REPORTING IN LOS ANGELES COUNTY: AN EVALUATION OF 1999 HOSPITAL DISCHARGE DATA

BACKGROUND

The California Health and Safety Code requires all suspected and confirmed pertussis cases among Los Angeles County (LAC) residents to be reported to the LAC Department of Health Services (DHS) within one working day of identification. Previous studies suggest that a substantial number of pertussis cases remain unreported, or are reported late to local health jurisdictions [1].

There are several reasons why suspect pertussis cases may not be reported. Some health care providers do not clearly understand the process of reporting cases to local health departments [2,3]. Also, some providers don't feel comfortable reporting unconfirmed cases [2]. Additionally, some providers are unaware of the important public health action that occurs when health departments receive timely notification about such cases [4].

A recent study found that doctors don't always consider the diagnosis of pertussis, even when an individual presents with classic symptoms [5]. According to the study, pertussis was considered in only 24-26% of children who met the case definition for pertussis [5]. Of the children who met the case definition, only 6% were reported to a health department [5].

Delayed and non-reporting can lead to "spread cases" resulting in significant morbidity and risk of death, especially for un-immunized infants. Timely reporting allows the local health department to ensure that close contacts to the suspect case receive prophylactic treatment and that the suspect case receives the appropriate antibiotic for the appropriate period of time. Additionally, preventing spread cases among contacts results in significant cost savings to society and reductions in parental time off from work. Average medical costs for treating an infant with pertussis are estimated at \$2,822, and the parent of a child with pertussis loses an average of 6 work-days caring for their child [6].

More than 60% of all pertussis cases, and 80% or more of affected infants, are hospitalized because of their illness. The extent to which LAC's current passive surveillance system is successful in identifying hospitalized pertussis cases is unknown. The goal of this study was to estimate the completeness of hospital reporting of suspect pertussis cases in LAC and attempt to identify hospitals that are non-adherent to the reporting requirement. The results of the study will be helpful in assessing the need for an enhanced surveillance system for pertussis in LAC.

METHODS

Office of Statewide Health Planning and Development (OSHPD) hospital discharge data from 1999 was reviewed for hospitals in LAC, Orange County, and San Diego County. Records with an LAC patient residence and a discharge diagnosis of "Bordetella pertussis" or "whooping cough, unspecified organism" were selected. A "unique identifier" (number based on a portion of the social security number) was available for 37% of the records and allowed 6 known duplicate records to be removed. The following method was used to estimate the maximum number of possible duplicate records among the remaining 63% of the records.

Records were matched on the basis of age of child at time of admission, sex, ethnicity, race, partial zip code, month of admission, and length of stay. Twenty-eight records were eliminated as possible duplicates (and 1 triplicate and 1 quadruplicate). The frequency of duplicates determined for this group was applied to a small unique set of records, which were not analyzable due to missing parameters.

By removing all possible duplicates, a “low estimate” number of LAC residents with a discharge diagnosis of “*Bordetella pertussis*” or “whooping cough, unspecified organism” was determined from the OSHPD data base. A “high estimate” number was also determined from the same data-base by removing only the duplicate records identified by use of the “unique identifier.” Both estimates were compared to hospitalized suspect cases reported to the LAC DHS during 1999, to determine the extent of under-reporting.

RESULTS

Based on OSHPD data the number of LAC residents with a pertussis “suspect” diagnosis was between 201 (“low estimate”) and 241 (“high estimate”). Only 154 hospitalized suspect pertussis cases were reported to LAC DHS in 1999. Thus, the percentage of hospitalized suspect cases reported to LAC DHS for this year ranged from 64% to 77% of the OSHPD estimate. Reporting varied substantially by hospital with some hospitals reporting all of their suspect cases while some reported none.

CONCLUSIONS

Although OSHPD data is limited by an inability to precisely identify duplicate records in the data base, the most conservative estimates, based on that data, document substantial under-reporting by hospitals of suspect pertussis cases in LAC. Specific hospitals were identified for targeting of interventions to improve reporting.

Interventions will include educating infection control practitioners, physicians, and nurses at the targeted hospitals about the importance of reporting all suspect pertussis cases. “Cite and fine” procedures, established by the California Medical Board for physicians, will also be implemented as appropriate when unreported cases are identified. LAC DHS staff will work with select hospitals to encourage implementation of hospital-based procedures to enhance the reporting of suspect pertussis cases.

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INVASIVE PNEUMOCOCCAL DISEASE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERNS FOR STREPTOCOCCUS PNEUMONIAE IN LOS ANGELES COUNTY, 2001

BACKGROUND

Streptococcus pneumoniae infection is a 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 in order to: measure the incidence in LAC, track antibiotic resistance patterns, potentially monitor immunization efficacy, and target vaccine usage.

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].

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 an increase of penicillin nonsusceptible *S. pneumoniae* isolates from 14% in 1993-1994 to 27% in 2000 [2,3]. Other classes of antimicrobials such as the macrolides, cephalosporins, and fluoroquinolones have also developed resistance.

The following is a description of the 2001 incidence of reported IPD and *S. pneumoniae* antimicrobial susceptibility patterns in individuals residing in LAC (excluding the cities of Long Beach and Pasadena).

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

Antimicrobial	MIC ($\mu\text{g/mL}$)		
	Susceptible	Intermediate	Resistant
Penicillin	≤ 0.06	0.12-1.0	≥ 2.0
3 rd generation Cephalosporin (cefotaxime, ceftriaxone, cefuroxime)	≤ 0.5	1.0	≥ 2.0
Erythromycin	≤ 0.25	0.5	≥ 1.0
Trimethoprim-sulfamethoxazole (TMP-S)	$\leq 0.5/9.5$	1/19-2/38	$\geq 4/76$

Table 2: Characteristics of IPD Cases Los Angeles County, 1997-2001

Characteristics*	1998 (N=814)	1999 (N=894)	2000 (N=760)	2001 (N=603)
Male:Female Rate Ratio	1.05:1.00	1.02:1.00	1.03:1.00	1.15:1.00
Age (years)				
Mean	44	47	43	51
Median	50	53	48	55
Range	<1 day-102	1 day-100	<1 day -101	1.5 mo. -103
Case fatality rate	15% (53/346)	17% (55/328)	13% (42/320)	15% (39/252)
Culture site				
Blood only	776 (96%)	836 (94%)	703 (93%)	540 (90%)
CSF/CSF&Blood	28 (3%)	44 (5%)	33 (4%)	34 (6%)
Other	10 (1%)	14 (2%)	24 (3%)	29 (5%)

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

METHODS

Cases were defined as LAC residents with a positive isolate for *S. pneumoniae* from a normally sterile site collected in 2001. To calculate incidence rates, population data were derived from the 2000 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 2000 and analyzed using Epi-Info 6.04 and SAS Version 8.02.

DATA ANALYSIS

The annual incidence rate of reported IPD decreased 31% from 9.8 cases per 100,000 (n=894) in 1999 to 6.8 cases in 2001 (n=603). As indicated by Table 2, the male-to-female ratios indicated that there were slightly more males who acquired IPD. In 2001, the mean age for IPD cases was 51 years (median 55 years, range 1.5 months to 103 years), which was higher than the previous three years.

In 2001, the case fatality rate was 15%, 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 2001 were reported as Aunknown®, 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. In 2001, a higher proportion of cases had cultures taken from the CSF and other sites such as chest fluid, pleural fluid, peritoneal fluid, and vitreous fluid than previous years. The mortality rate in 2001 was not significantly associated with having meningitis (odds ratio [OR]: 2.10; 95% confidence interval: 0.82 to 5.21, p=0.26).

For 2001, the highest age-specific incidence rates occurred in adults' 75 years and over, which is common with IPD. LAC data also shows a noticeable decrease of IPD in children <5 years for 2001 (Figure 1).

The IPD cases for 1997-2001 followed the typical seasonal pattern, peaking in late winter then gradually declining through spring. The pattern observed by month for the first three quarters in 2001 was very similar to previous years but cases started to deviate from October to December from the normal pattern seen in previous years (Figure 2).

In 2001, Harbor District had the highest crude rate of IPD at 14.3 per 100,000 population (28 cases) followed by Southwest with a rate of 10.8 (39) and Torrance with 9.0 (39). The West Valley District had the highest number of cases (40). Harbor District continued to have the highest rate (12.9 cases per 100,000) even after adjusting for age (using

Figure 1: Incidence Rates of IPD Cases by Age, Los Angeles County, 1997-2001

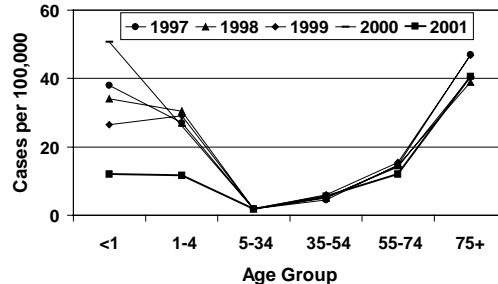


Figure 2: IPD Cases By Month of Culture Los Angeles County, 1997-2001

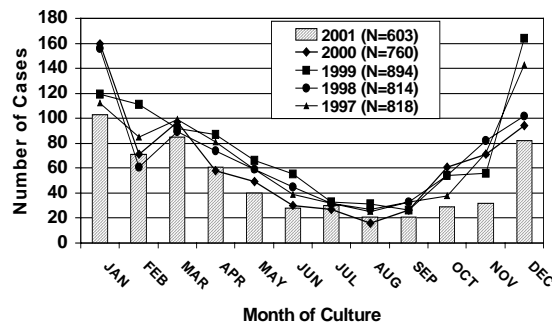
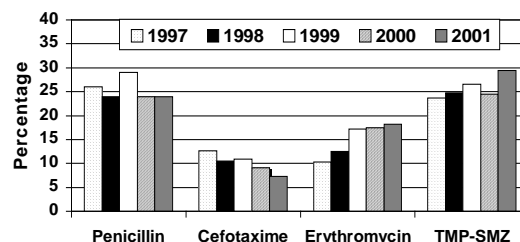


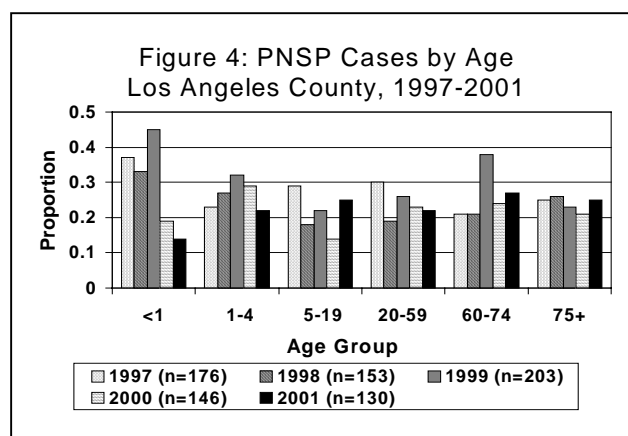
Figure 3: IPD Cases Nonsusceptible to Selected Antimicrobial Agents Los Angeles County, 1997-2001



the age groups in Figure 1). For 2000, Harbor District was also among the top five districts for crude and age-adjusted rates.

From 1997 to 2001, the proportion of penicillin nonsusceptible *Streptococcus pneumoniae* (PNSP) isolates has remained stable at around 24% for all years except for 1999 (29%) (Figure 3). Ninety-three percent of the cases had antimicrobial resistance information provided. The fluctuation of PNSP by year was not significant ($\chi^2=7.98$, p-value=0.09). The percent of cases nonsusceptible to erythromycin and trimethoprim-sulfamethoxazole (TMP-SMZ) increased from 1997 to 2001 and cefotaxime decreased. Of the 212 cases with data on levofloxacin resistance, only 1% were nonsusceptible which is greater than 0.3% seen in 2000 from a nationwide population-based surveillance system for IPD [3].

From 2000 to 2001, the proportion of PNSP cases did not fluctuate greatly for most of the age groups. The largest increase of 79% was observed in the 5-19 age group but was similar to previous levels (Figure 4). Comparing 2000 and 2001 to 1999, there has been a large decrease (68%) in the proportion of PNSP cases in children less than one year. In 2001, there was not a significant difference between age groups and penicillin nonsusceptibility ($\chi^2=1.63$, p-value=0.90). Also mortality was not significantly associated with penicillin nonsusceptibility.



DISCUSSION

Compared to previous years, the DHS observed a decrease in IPD incidence in 2001 while the resistance pattern toward selected antibiotics varied. Once again the elderly were at a higher risk of acquiring IPD. Unlike previous years, there was a dramatic decrease in the incidence of IPD in children less than five years, which may be attributed to the use of the newly licensed pneumococcal conjugate vaccine. Resistance was not associated with increased mortality.

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AN OUTBREAK OF MULTI-DRUG RESISTANT SALMONELLA NEWPORT

Through routine surveillance, the Acute Communicable Disease Control Unit (ACDC) noted in June 2001 a cluster of seven *S. Newport* isolates from persons with illness onset in late May, 2001. A review of routine salmonellosis case history forms revealed no common restaurants, food items or other risk factors. All cases were Hispanic and 5/7 cases were adult women. On June 15, 2001, an investigation was initiated to determine if the cases were associated with a common source and if control measures were needed.

METHODS

Cases were defined as ill persons with a culture positive for *S. Newport* with onset of symptoms between May 15 and June 15, 2001. Case ascertainment was conducted through bacteriology laboratories in Los Angeles County (LAC) which were asked to expedite submission of *Salmonella* Group C2 isolates to the Public Health Laboratory (PHL). The PHL gave priority to serotyping of *Salmonella* Group C2 isolates. *S. Newport* isolates were then subtyped by pulsed field gel electrophoresis (PFGE). The California DHS and other local health departments were asked if they were also seeing an increase in *S. Newport* cases during the outbreak period. Routine salmonellosis case history forms were reviewed, and demographic variables were described.

A case-control study was conducted. For the purposes of the case-control study, cases were defined as ill persons with a positive culture for *S. Newport* between May 15 and June 15, 2001 whose isolates matched the CDC PulseNet "PFGE pattern 14," which is a multi-drug resistant strain. We used a standard hypothesis-generating questionnaire. Five LAC cases were interviewed by telephone or in person using comprehensive questionnaires which reviewed food history, exposures to animals, pets, travel, and medical conditions. Items to which more than 50% of the cases had exposure were included in the case/control study questionnaire. Case and control questionnaires and a protocol for finding controls were developed. The remaining cases were interviewed in person using the case control questionnaire, which included food and drink items, travel, animal exposures and medical history. For each case in the study, three controls were selected by systematic protocol and interviewed in person. Controls were age matched, and did not have diarrheal illness within the past two months. Controls were administered the control questionnaire, which asked the same exposure questions. Data was analyzed using Microsoft Access 2000 and EpiInfo version 6.

The LAC isolates were serotyped in the LAC PHL. All LAC isolates were subtyped by PFGE. Cases with non-outbreak subtypes of *S. Newport* were not included in the case-control study analysis.

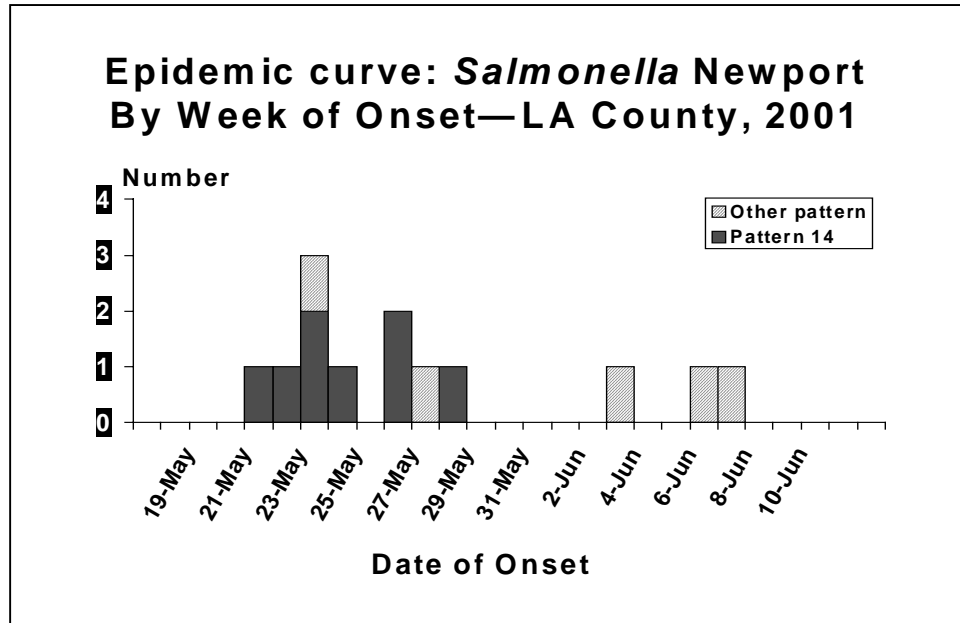
RESULTS

Isolates were obtained from 14 persons with *S. Newport*, who had onset of symptoms between May 15 and June 15, 2001. All isolates were from feces. All isolates were confirmed and subtyped in the LAC PHL. Thirteen isolates were from LAC residents, one from an Arizona resident who was staying in LAC at the time of the outbreak. PFGE subtyping showed that 8 isolates were from persons who had PulseNet pattern 14" and were deemed part of the outbreak, while six isolates were different from the outbreak strain. These six persons were eliminated from the case control study analysis. Other background isolates from previous years also differed from the outbreak strain. Consultation with other local health departments and the California DHS revealed no additional cases.

Case interviews were completed for 11 of 14 persons with *S. Newport*. Three people were not interviewed when we learned that they were not part of the outbreak. Eight cases were included in the case control study. All of the six excluded cases (including one of the hypothesis-generating interviews) did not have the outbreak subtype on PFGE analysis. Of the eight persons who were outbreak cases, six were females, and all were Hispanic ethnicity and white race. The mean age was 26 years, with a range from two

to 67 years old. All 8 cases had onset of illness between May 19 - 27, 2001. Three of the cases were hospitalized. Symptoms reported included diarrhea in 100%, including 25% with bloody diarrhea, abdominal cramps in 75%, fever in 63%, vomiting in 38%, headache in 13%, myalgia in 13%. Two cases were hospitalized; a third case developed postpartum fever and diarrhea and remained in the hospital beyond the routine 48 hours.

The only food item associated with *S. Newport* infection was cilantro; on matched analysis of 8 cases and 24 controls, the p value was 0.059. All cases reported eating cilantro. All 8 of the cases were Hispanic ethnicity, while only 12 of the controls were. When race was controlled for in the analysis, cilantro dropped out as a suspect food item, with a p value of 0.66.



After consultation with the California DHS, a cilantro trace back not done because the results of our matched case-control study were not significant, there were a small number of cases, and the outbreak ended on its own before any intervention was carried out.

CONCLUSIONS

Cilantro appears to be the source of infection in this widespread outbreak. No other food item is implicated. The preponderance of Hispanic cases is typical of outbreaks due to cilantro, which are often consumed on various foods. No other foods typically found as sources for *S. Newport* outbreaks, such as raw milk, cheese made from raw milk, ground beef or chicken were implicated.

This Multi-drug resistant subtype of *Salmonella Newport* has been found sporadically in LAC since 1999. In 2000, an outbreak of this MDR serotype was found to be associated with consumption of goat meat.

2001 SN Outbreak Results (N= 8 cases, 24 controls)

Food Eaten	% Cases	McNemar p-value
Cilantro	100 (8)	0.059
Grape Juice	50 (4)	0.35
Chicken	100 (8)	0.44
Raw Milk Cheese	13 (1)	0.56
Mango	50 (4)	0.63
Eggs	75 (6)	0.65
Beef	75 (6)	0.78
Ground beef	63 (5)	0.83
Goat	13 (1)	1.0

WASH THAT PRODUCE! OUTBREAKS OF SALMONELLOSIS IN 2001 ASSOCIATED WITH RAW PRODUCE

SUMMARY

Raw fresh produce was implicated in six of ten salmonellosis outbreaks in Los Angeles County (LAC) in 2001. Five of the six outbreaks were also part of multi-state or multi-county outbreaks. In all six outbreaks, case-control studies were conducted to determine risk factors for becoming infected. LAC Acute Communicable Disease Control (ACDC) conducted its own case-control study for a local outbreak; otherwise, these studies were conducted at the state level. LAC cases were included in all case-control studies. Pulsed-field gel electrophoresis analysis was conducted in the PHL and the State Microbial Disease Laboratory (MDL) on all human isolates and some environmental samples. In some situations, non-human samples were processed at the Food and Drug Division lab in Southern California. All cases (and some environmental samples, if collected) in these outbreaks were indistinguishable by PFGE analysis. Trace back investigations were conducted in the five multi-state or multi-county outbreaks. The infected produce in the LAC 2001 outbreaks included alfalfa sprouts, cantaloupe, pre-cut melon, cilantro, and green grapes.

In each of these outbreaks, a case was defined as a person with a laboratory confirmed culture of the serotype associated with the outbreak during the timeframe of the outbreak. In addition, the PFGE pattern must be indistinguishable from the outbreak pattern. The PFGE patterns were posted on PulseNet, the national molecular subtyping network for foodborne disease. The sharing of PFGE patterns between participating laboratories in the US and Canada is helpful in determining if a cluster of illness is a local problem or involves multiple parts of the country.

LAC Department of Health Services (DHS) Public Health staff assisted the State in these investigations by notifying the California Department of Health Services (CDHS) of possible cases cultured in the LAC Public Health Laboratory (PHL), and by administering outbreak questionnaires to LAC cases. These questionnaires, as well as all LAC case investigation forms, and the results of PFGE analysis conducted by the PHL were forwarded to the CDHS.

Outbreak 1: *Salmonella* serotype Kottbus associated with consumption of alfalfa sprouts (February to April 2001). In mid-March 2001, both ACDC and the CDHS identified a cluster of *Salmonella* Kottbus (SK) isolates with indistinguishable PFGE patterns. SK is a rare serotype in California as well as in the rest of the US. The health departments of other western states were notified about the cluster, and were asked to forward SK isolates to the MDL for PFGE analysis. After a case-control study conducted by CDHS found alfalfa sprouts to be significantly associated with illness, a trace back investigation was initiated. As a result of this investigation, a single sprout producer in LAC was identified as the source of the contaminated sprouts, and eventually a single seed lot was implicated. The seeds from the infected lot were imported from Australia in November 2000. Multiple environmental samples from the seed production plant were collected. On April 17, the sprouter issued a voluntary recall.

Twenty-four cases of SK (23 from California, and 1 from Arizona) were found to be associated with this outbreak. Cases occurred from the beginning of February through May 1, 2001. Seven of the 23 cases were from LAC. The median age of the cases was 36 years (range: 9-72 years); median age of the LAC cases was 31 years (range 21-67 years). 67% of the cases were female (LAC: 100%). Three cases had urinary tract infections (2 from LAC); three cases were hospitalized (1 from LAC). There were no deaths. PFGE patterns of the SK isolates, as well as ungerminated seeds, and floor drain samples from the seed production plant, were indistinguishable. No method currently available reliably eliminates all pathogens that may be present on sprout seeds. The sprouter was not following the CDHS recommendations for sprout seed decontamination with a 20,000 ppm hypochlorite. At present, this process has been found to be the most effective decontamination method.

Outbreak 2: *Salmonella* serotype Poona (H2S negative) associated with consumption of cantaloupe (April to May 2001). In late April 2001, CDHS Disease Investigations and Surveillance Branch (DISB) reported a cluster of laboratory-confirmed cases of hydrogen disulfide (H₂S)-negative *Salmonella* serotype Poona (SP). H₂S negative SP is an unusual biochemical variant; H₂S positive is the usual biochemical pattern. The initial eight cases identified had a Pulsed-Field Gel Electrophoresis (PFGE) pattern indistinguishable from each other.

Cases were identified throughout the US (NV, AZ, OR, WA, CT, GA, LA, MA, MO, IL, NM, NY, TN) and a few in Canada. The State investigation identified 28 cases in California (7 in LAC residents). All seven LAC cases had a PFGE pattern that was indistinguishable from the outbreak pattern. LAC cases occurred from April 8-May 21 (six of seven had onset between April 8-28). Age range for the LAC cases was 9 months to 2 years (median: 1 year). Four (57%) of the LAC cases were male. Two of seven (29%) had positive blood cultures; two of seven (29%) were hospitalized. There were no deaths in LAC cases.

Results of the case-control study conducted by the DISB linked consumption of cantaloupe to illness. Two press releases were issued:

1. May 15, 2001 by the CA DHS recommending that consumers wash cantaloupe prior to eating.
2. May 25, 2001 by the U.S. Food and Administration (FDA) warning consumers about cantaloupe contaminated by SP.

The trace back investigation implicated a Mexican farm source. Two previous multi-state outbreaks of SP have occurred in the last ten years: June 1991 (>400 confirmed cases from 23 states), and April 2000 (46 cases). Both outbreaks were found to be associated with the consumption of cantaloupe. A trace back during the April 2000 outbreak found the source of the infected cantaloupe was also from Mexico.

Outbreak 3: *Salmonella* serotype E1:e,h:- (untypeable) associated with consumption of cantaloupe (April to June 2001). During April and May 2001 CDHS MDL reported a cluster of 12 *Salmonella* E1:e,h:- (untypeable) cases, most from southern CA. After posting the PFGE pattern on PulseNet, other cases were found in Utah (2), Oregon (1), and Idaho (1). An additional case from Canada (British Columbia) was also identified. A case-control study showed that consumption of pre-cut cantaloupe purchased in a grocery store or eaten in a restaurant was significantly associated with illness. Consumption of any cantaloupe purchased either pre-cut or whole (and cut later) was also a risk factor for illness. LAC had 3 cases associated with this outbreak. Two of three were female; ages were 32 years (male), 67 years and 72 years. Median age in the case-control study was 60 years. None of the LA cases were hospitalized, and none died. All of the LAC cases had PFGE patterns indistinguishable from the outbreak strain. However, two LAC cases had symptom onset somewhat earlier than those associated with the outbreak (i.e. onset from April 1). The 2 LAC women had onset February 15 and March 3. Cantaloupe collected in CA tested positive for *Salmonella* E1:e,h:- as well as for *Salmonella* Anatum. An outbreak of *Salmonella* E1:e,h:- occurred at the same time in 2000, and had the same PFGE pattern as in 2001. The outbreak in 2000 involved the western states. A trace back investigation of the cantaloupe was conducted by the CDHS Food and Drug Branch and the Food and Drug Administration.

Outbreak 4: *Salmonella* serotype Newport associated with consumption of cilantro (May 2001). In June 2001, ACDC noted a cluster of *Salmonella* Newport isolates from persons with illness onset in late May. When no common risk factors were identified, a case-control study was initiated. This cluster of *S.* Newport involved only LAC. The isolates were indistinguishable from CDC PulseNet "PFGE pattern 14", a multi-drug resistant strain. Eight persons were identified as outbreak cases. All were Hispanic; six were female. The mean age was 26 years (range: 2-67 years). All had illness onset between May 19-27. Two were hospitalized; there were no deaths. The only food item identified as significant was cilantro; however cilantro was not significant when race was controlled in the analysis (only 12 of 24 controls were Hispanic). A trace back was not done as the results of the case-control study were not significant, and the outbreak ended before any intervention was done.

Outbreak 5: *Salmonella* serotype Poona (H2S positive) associated with consumption of cut-off-the-rind melon (May to June 2001). In mid July 2001, CDHS noted an increase in *S. Poona* (H2S positive) throughout the month of June. About 66% of the isolates were from southern CA counties; the rest from northern CA. This outbreak involved H2S positive cases rather than H2S negative cases that were seen in the April-May outbreak. CDHS conducted a case-control study, and found an association between illness and eating pre-cut-off-the-rind melon (cantaloupe, honeydew, watermelon). There was no statistically significant association between illness and eating cantaloupe in general. Twenty-five cases in CA and four from out of state (MA, GA, KS, WA) had a PFGE pattern indistinguishable from the outbreak strain. All out of state cases had visited southern CA except the case from KS. Six of the CA cases were from LAC. All LAC isolates were feces except for one culture of a vaginal abscess. Onset dates for the CA cases range from June 1-June 26 (LAC cases: June 1-June 15, except for the case with a vaginal abscess who reported onset 12/00, although her culture date was 6/13). The age range is from 1-64 years (LAC: 1-40 years, median 2). Most cases are White, non-Hispanic (LAC: 1 Hispanic, 4 White non-Hispanic). Four (67%) of the LAC cases were female. Two LAC cases were hospitalized; there were no deaths. The results of the trace back are not known.

Outbreak 6: *Salmonella* serotype Senftenberg associated with consumption of green grapes (September to December 2001). In mid October 2001, CDHS noted a cluster of 10 *S. Senftenberg* cases with specimen collection dates between September 14-October 3 occurring throughout the state. Hypothesis generating interviews did not find anything significant. Cases with indistinguishable PFGE patterns were found in four western states (CA CO, NV, AZ). A case-control study was initiated with Colorado taking the lead. Most of the outbreak related cases had onset in September and October. A total of 41 cases in the western states cases were linked to the outbreak; the majority were in CA (17) and CO (15). Of the 17 cases in CA, six were in LAC; five of the six LAC cases had onset from September 17-October 21 (four had onset from October 10-21). The sixth case had onset December 5. The median age for the outbreak was 28 years (range 2-79) with 54% female. In LAC the median age was 15.5 years (range 2-48) with 67% male. All LAC isolates were stool. LAC had no hospitalizations and no deaths. The case-control study found consumption of green grapes to be significant. The FDA conducted a trace back investigation; results were inconclusive. In autumn, most grapes are from CA.

DISCUSSION

Since 1995, an increasing number of outbreaks have been associated with fresh produce. *Salmonella* outbreaks caused by mangoes and unpasteurized orange juice have occurred in the recent past. In addition to *Salmonella*, outbreaks of *E. coli* 0157:H7 have been associated with alfalfa sprouts, and outbreaks of *Shigella sonnei* have been associated with fresh parsley. Contamination of the produce can occur in the field where it is grown, during harvesting or transport, or during preparation (e.g. cutting or chopping). Washing fresh produce before consumption can be helpful in some instances, e.g. cantaloupe. However, washing may be ineffective in other instances, e.g. alfalfa sprouts, as the sprout itself may be infected. The public may be more aware of the problem due to publicity when large outbreaks occur. However, because produce is considered a healthy food, and some feel there is no risk with “organic” produce, proper precautions are often not taken. Young children, the elderly, and the immunocompromised should avoid high-risk items like alfalfa sprouts or unpasteurized juices. Yet these are the groups who often choose such items due to perceived health benefits.

The use of PFGE has been crucial in identifying outbreaks. The sharing of PFGE patterns on PulseNet has assisted in the identification of national and international outbreaks. Such connections could have been easily missed in the past.

SHIGELLA SONNEI ASSOCIATED WITH A SMALL MEXICAN RESTAURANT

BACKGROUND

On September 24, 2001 the District Public Health Nurse (PHN) notified ACDC of four cases of shigellosis (due to *Shigella sonnei*) living in close geographic proximity and having close onset of illness dates. The PHNs early investigation results determined that at least two of these cases had eaten at a the same Mexican restaurant in West Los Angeles.

CASE DEFINITION

A case of outbreak-associated shigellosis was defined as: 1) either a person with culture-confirmed *Shigella sonnei* infection or symptoms of diarrhea and fever, and 2) a history of consuming food at the suspected Mexican restaurant between September 16, 2001 and September 22, 2001 – the incubation period.

METHODS

The district PHN and ACDC accompanied Environmental Management on an inspection of the restaurant. All employees were required to complete a questionnaire regarding job duties, work hours, and illness and to submit stool specimens for culture. A list of all dining partners and foods eaten was obtained from confirmed cases. A standard questionnaire regarding symptoms and foods eaten was administered to each diner. Additional case finding methods including sending letters and a supplemental questionnaire requesting additional information on *Shigella sonnei* cases or *Shigella*, unspecified infection cases with onsets during September to district health centers and routine surveillance of *Shigella* cases and Food-borne Illness Incident (FBI) reports. Available *Shigella* isolates from outbreak-associated cases were submitted from provider laboratories for Pulse Field Gel Electrophoresis (PFGE). The state health department was contacted to determine if cases in other jurisdictions could be related to this outbreak.

RESULTS

Environmental: A multidisciplinary team inspected the restaurant on September 25, 2001. Problems noted during the inspection included unclean surfaces and equipment, handwashing violations and improper sanitizing. Employees stated all items, including salsas, were made fresh daily. Ingredients, including cilantro and onion, were delivered on Friday, September 14, 2001 and again on Tuesday, September 17, 2001 from a Los Angeles warehouse. Environmental health investigators inspected the Los Angeles produce warehouse supplying the restaurant with both cilantro and onion. This inspection revealed multiple problems including standing water, no drains of any kind, a nearby room where garbage and rotten produce was accumulating, and condensate dripping from the ceiling onto produce. Due to these findings, the Los Angeles produce warehouse was closed down pending a hearing with Food and Milk Program.

Epidemiology: In total, 22 persons from 12 dining parties were exposed. From the known exposed group, 18 individuals met an outbreak case definition. Thirteen persons were culture positive for *Shigella sonnei*, and five persons met the clinical case definition for shigellosis. Four exposed persons did not report illness and were used as the comparison group. Reported onset dates of cases ranged from Monday, September 17, to Saturday, September 22, with most cases having onset on Wednesday, September 19. Reported exposure dates ranged from Sunday, September 16, to Thursday, September 20, with most exposure (72 %) occurring on Monday, September 17. A case-control study was performed to compare food consumption history differences; however, with only four identified controls, statistical power was limited. The only statistically significant food item was salsa roja, but it only accounted for 69 % of cases. When food items were broken down into individual ingredients, cilantro and onion were significant. These two ingredients (which were in the pico de gallo) could account for 100 % of the illness.

All employees at the restaurant denied symptoms of disease for themselves and their household contacts. No single employee worked all of the of exposure days reported by the cases.

Laboratory: All employees tested negative for *Shigella*. PFGE analysis was performed on six available case isolates. Four isolates shared one pattern and two shared a second pattern. These two patterns have a three-band difference from each other and are both common to Southern California.

The state health department did not identify any other cases associated with this outbreak. No produce trace back was initiated.

CONCLUSIONS

This outbreak was identified through disease-specific surveillance of shigellosis cases. The epidemiological curve indicates that there was a common source for this outbreak. It is less likely that an employee was this common source; all employees tested negative, multiple foods were not implicated and no single employee worked all days of exposure. Cilantro or salsa containing cilantro has been associated with *Shigella* outbreaks in the past. Although two ingredients, onions or cilantro, were identified as statistically associated with illness, the source of the contamination could not be determined. Poor conditions at the Los Angeles warehouse may be contributory. A three-band variation in PFGE patterns within outbreaks of *Shigella* is expected, however, having a common pattern limited the ability to utilize this technology to pinpoint other related cases.

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**RISING RATES AND SHIFTING SEROTYPES:
SHIGELLOSIS IN MEN WHO HAVE SEX WITH MEN – LOS ANGELES COUNTY, 1998 - 2000***

BACKGROUND

Shigellosis is a febrile gastrointestinal illness caused by one of the four common species, or serotypes, of the pathogenic *Shigella* bacterium—*S. sonnei*, *S. flexneri*, *S. boydii*, and *S. dysenteriae* [1]. Transmitted through the fecal-oral route, *Shigella* has a small infective dose of 10-100 organisms and so it can be easily spread person-to-person, via contaminated fomites, or by ingestion of contaminated food or water. In Los Angeles County (LAC), highest rates are usually seen in young children, aged 1-4 years and as outbreaks in daycare settings. *S. sonnei* has for years been the most common serotype found in LAC. In 1999, routine surveillance showed a high incidence of *S. flexneri* in men who reported having had sex with men (MSM), while for 2000, *S. sonnei* cases predominated.

The objectives of this study were to: 1) identify risk factors and characterize the distribution of serotypes among LAC adult male shigellosis cases, and 2) to determine if men who have sex with men (MSM) are at higher risk for acquiring *Shigella* than men who report having sex with women exclusively (MSW).

METHODS

Using the LAC Public Health passive surveillance database, we identified shigellosis cases among LAC adult males, defined as aged 15 years and older, with an onset of illness between 1998 and 2000. All shigellosis cases were interviewed by public health nurses using a routine case history form. Variables obtained included demographics, serotype, and reported gender(s) of sexual partner(s), if any. Analysis included incidence rates, rate ratios, and proportional morbidity ratios. Population estimates were obtained from the 1999 Urban Research database and proportion of MSM among LAC adult males was estimated using results from the 1999 Los Angeles Health Survey.

RESULTS

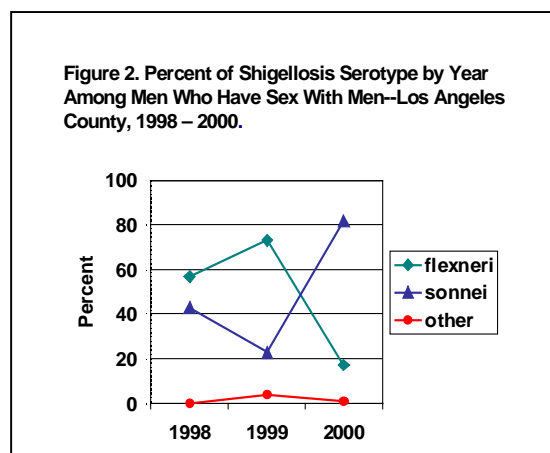
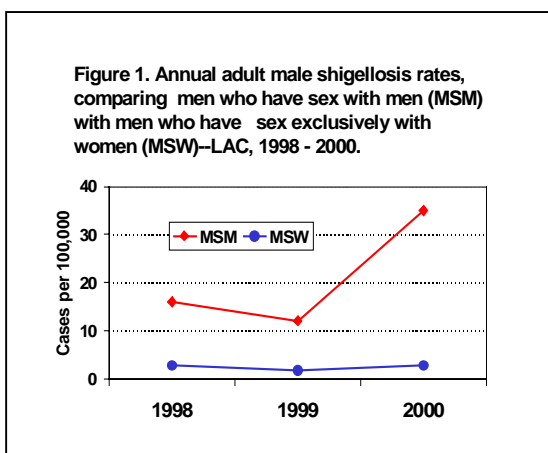
Of 2,266 cases of shigellosis reported from 1998-2000 in LAC, 527 (23%) were adult males. Of these, 29% (154) identified as MSM, 46% (240) as MSW, while 25% (132) did not report the gender of any sexual partner. Characteristics of adult male cases are shown in Table 1. For the three years of data combined, MSM did not differ from MSW by age or serotype. However, there were significantly more white and fewer Hispanic MSM cases than MSW cases. And the rate of disease incidence was 8.5 times higher for MSM (28 per 100,000) compared with MSW (3.3 per 100,000).

Table 1. Characteristics of Adult Male Shigellosis by Known Sex-partner Gender—Los Angeles County, 1998 – 2000 (n = 394).

Characteristic	MSM	MSW	Significance
Age: (years)	37 (17-83)	39 (15 – 96)	--
Race/ Ethnicity			
White, non-Hispanic	71%	36%	p<0.0001
Hispanic	21%	51%	p<0.0001
Black	6%	21%	p=0.3
Other/Unknown	2.5%	4%	--
Serotype			
<i>S. Sonnei</i>	55%	50%	p=0.3
<i>S. Flexneri</i>	34%	33%	p=0.9
Other/Unknown	11%	17%	--
Rate: (per 100,000)	28	3.3	RR=8.5 [6,12]

While rates for MSW remained stable throughout the three-year period, MSM rates more than doubled in 2000 (35 per 100,000) from the previous two years (16 and 12 per 100,000, respectively), as is shown in Figure 1. Further, while MSW cases were predominantly *S. sonnei* throughout the study period, cases among MSM were more than half *S. flexneri* in 1998-1999, then 75% *S. sonnei* in 2000 (see Figure 2).

* Authors include: Douglas M. Frye, M.D., M.P.H., Rachael Zweig, M.P.H., Jacqueline Vogt, R.N., B.S.N., Karl Kabase, M.D., M.P.H., and Laurene Mascola, M.D., M.P.H.



DISCUSSION

In LAC for 1998-2000, men who reported having had sex with men, including bisexual men, had an eight times higher risk for coming down with shigellosis than were men who reported having sex with only women, the annual rate for MSM more than doubled in 2000 from previous years, and *S. sonnei* replaced *S. flexneri* as the predominant serotype in MSM in 2000.

Limitations of our study include the gross under-reporting of *Shigella* cases to public health officials by clinicians [2]. Also, in both shigellosis case history forms and in the L.A. Health Survey, about 25% of respondents did not specify the gender of their sexual partner(s). This would likely have the effect of under-estimating both the numerator and denominator of disease among MSM. Finally, differential biases were possible in the detection and reporting of shigellosis cases, both by race/ethnicity and by gender of sexual partner. For instance, it may be that White, Hispanic males were less likely to report MSM than were White, non-Hispanic males. It is unclear what effect this may have had on estimates of significant findings.

Increased incidence of shigellosis among MSM was first seen in the late 1970's [3]. *S. flexneri* was the predominant serotype then, as it was for LAC in 1999. In recent studies, Vugia et al found an association of *S. flexneri* infection and MSM, HIV, AIDS, and oral-genital sex in a study of San Francisco adults in 1998 – 1999 [4]. In the last half of 2000, San Francisco also investigated an outbreak of *S. sonnei* among MSM [5]. In 2001, PFGE-indistinguishable clusters of *S. sonnei* were seen in MSM both in Victoria, British Columbia, Canada and in LAC [6,7].

RECOMMENDATIONS

Our findings led to the following public health actions: a letter was drafted and sent to area health officers and nursing managers requesting that public health nurses ask about and fill out the sexual partner question on all case history forms of cases aged 15 years and older; a press release warning gay men about shigellosis was drafted and sent to the gay media; and a “plain-talk” brochure was developed targeting gay men and their risk for contracting shigellosis.

Public health jurisdictions with a substantial MSM population should consider including sexual risk factors, sexual partner gender, and recent travel histories in their routine shigellosis surveillance case history forms and databases. They should adopt pre-existing, or develop their own, educational materials that target MSM.

Clinicians should obtain stool and/or blood specimens for their patients with febrile and/or bloody diarrheal illness. When enteric pathogens are found, these should be reported to the health department by the clinician—as shigellosis is not yet a laboratory-reportable illness in California.

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EFFECT OF SCHOOL EXCLUSION ON A VARICELLA OUTBREAK IN A HIGHLY IMMUNIZED POPULATION

BACKGROUND

In 2001, the state of California mandated varicella vaccination for all children entering pre-school or school for the first time. This new law has raised many interesting questions about school exclusion policies for both non-vaccinated healthy children and all ill children during varicella outbreaks.

Non-vaccinated (“susceptible”) children who are kept home when an outbreak occurs may avoid illness and prevent transmission of disease, but also may miss many days of school since outbreaks can last several weeks or months. A strict policy of exclusion may provide incentive for parents to have their children vaccinated if they know the child will be forced to miss school during an outbreak.

The process of exclusion of children who develop disease during an outbreak has changed with changing disease patterns following vaccination. Previously, it was standard to keep all children with varicella home for 5 days. The current understanding is that children must stay home until all lesions have crusted over. However, there is no standard policy uniformly supported by health care workers or school administrators, with respect to vaccinated (“breakthrough”) cases of varicella where the children often do not develop lesions which crust over.

When an outbreak of varicella occurred in a Los Angeles County elementary school, we investigated to determine whether low vaccine coverage or vaccine failure was responsible, to compare illness in vaccinated versus non-vaccinated children, and to evaluate whether the suggested policy of excluding susceptible children during an outbreak was appropriate.

METHODS

The case definition was defined as an acute maculo-papulo-vesicular rash with no other diagnosis occurring in a child attending the school from September 1, 2001 through January 12, 2002. A susceptible child was one with no history of either vaccination or natural disease. The exposure group was children sharing a classroom with a case-patient. Questionnaires were administered to parents of exposed children and an in-depth telephone questionnaire was administered to parents of cases. School immunization records were reviewed and vaccination dates confirmed with the provider, when necessary.

RESULTS

The involved elementary school had 982 students in grades K through 6. The outbreak spanned 93 days, involved 21 of 44 classrooms, and 417 exposed children. Information was collected on 387 children (93% response rate), including 48 of 51 case-patients. 341 (88%) of children had been vaccinated or had a history of disease. The vaccine effectiveness was 86%, within the expected range of 70% to 90%. Susceptible cases (n=19) were more likely than vaccinated cases (n=24) to have >50 total lesions (relative risk [RR] = 3.8; p-Value [p] = 0.002), to have vesicles present (RR = 1.4, p = 0.023), and to report fever (RR = 2.1; p = 0.023), all markers of disease severity. Susceptible and vaccinated cases both missed a median of 5 days of school. However, the susceptible case-patients had longer duration of their rash and spent more days feeling “sick.”

There were three cases of secondary spread to mothers of children attending the school. Their mean age was 37 years old (range, 28 to 45 years) and two were healthy non-vaccinated women with no varicella history. One was an immunocompromised woman with only one of two recommended varicella vaccina-

tions who had never had varicella. Additionally, another mother's primary care physician initially did not recommend vaccination despite antibody negative serology.

CONCLUSIONS

The outbreak duration and illness occurring in a highly vaccinated population indicate that exclusion of susceptible children during an outbreak would not have been practical. The parents involved in this outbreak who had not vaccinated their children had made an informed decision and due to the year-round academic calendar at this school, most families have alternate caregivers to accommodate long periods of time off from school throughout the year. Many of these parents may not have vaccinated their children even under the threat of missed school days. This exclusion practice should be reconsidered once there are fewer outbreaks and fewer cases due to increased population of school children who have been adequately vaccinated.

Although all cases missed the same number of school days, vaccinated cases were less ill than susceptibles. One of the initial arguments for varicella vaccination was that it would prevent parents from missing days of work due to a sick child. In this outbreak, this did not hold true. Breakthrough cases presented with both fewer lesions and fewer vesicles. It is assumed that these children are less contagious than susceptible children. In the vaccinated children who develop only macules, a policy allowing them to return to school after 48 hours with no new lesions should be considered.

This varicella outbreak occurred among a population with a high disease protection rate, and the vaccine functioned within the reported effectiveness range. Therefore, the outbreak was not due to either vaccine failure or failure to vaccinate.

Regardless, routine varicella vaccination and education about occurrence of vaccinated cases should continue. The importance of education of medical providers for adults, as well as children, is exemplified by the adult cases which occurred in relation to this outbreak. Parental varicella history, antibody testing, and vaccination should be considered.

***Aedes albopictus* IN LOS ANGELES COUNTY**

In June 2001, the Los Angeles County (LAC) Department of Health Services (DHS) received notice from Centers for Disease Control and Prevention (CDC) quarantine office at the port of San Pedro and the Greater Los Angeles County Vector Control District (GLACVCD) that *Aedes albopictus*, commonly known as the Asian tiger mosquito, had been found in a shipment of "Lucky Bamboo" (*Dracaena* spp.). This plant is an ornamental and was shipped in small pots with 2 to 3 inches of standing water to keep them green on the ocean voyage [1]. All stages of mosquito development were found in these containers. *Ae. albopictus* feeds during the day and can transmit diseases such as eastern equine encephalitis, La Crosse encephalitis, and dengue fever.

For this reason, on June 29, 2001, CDC imposed an embargo on the importation of *Dracaena* spp. via containerized cargo in order to halt the introduction of more *Ae. albopictus* into California [1]. *Ae. albopictus* has been found in the eastern United States since 1985 when it was first discovered in Houston, Texas, after being imported inside used tires. This mosquito adapts well to breeding in many different types of containers, both man-made and natural, such as flowerpots, cans, tree holes, and cemetery urns. Also, water supplied by irrigation may provide primary breeding sites. Since 1985, it has been found as far north as Chicago, Illinois, and as far east as New Jersey. The mosquito has also become established in Missouri and Kansas, confining itself to wetter microclimates in parks and neighborhoods [2].

The mosquitoes had sufficient time to establish themselves at various local nurseries in LAC. Seven nurseries were infested by *Ae. albopictus* when port authorities, CDC and GLACVCD investigated. These infestations lasted at least three months near some of the nurseries and eggs were found 1,000 meters from the original site [1]. However, these eggs were not viable.

LAC has a dry, desert-like climate that is not as conducive to the growth of mosquitoes as the more humid eastern states, yet *Ae. albopictus* has managed to establish itself in the moister climates of watered parks and neighborhoods in Missouri and Kansas. Early evidence suggests that it is able to live within the moist environment of a nursery in Southern California [1]. It is not unreasonable to suggest that they could establish themselves in parks and neighborhoods in LAC for the same reasons.

Since 2001, there has been an ongoing outbreak of dengue fever in Hawaii and epidemics of this disease occur in many other parts of the world. Infected individuals traveling from Hawaii or other countries could serve as a source of dengue, which could then be transmitted by *Ae. albopictus* here in LAC, to local residents.

With heavy traffic into LAC via the Los Angeles International Airport, the LAC DHS should be alert to the possibility that dengue fever or other diseases transmitted by this mosquito, could occur locally in LAC.

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ACUTE COMMUNICABLE DISEASE CONTROL PROGRAM

Acute Communicable Disease Control Program	Laurene Mascola, MD, MPH
- Support Services Unit	David Dassey, MD, MPH
- Enhanced Surveillance Project.....	Irene Culver
- Hospital Outbreaks & Bloodborne Pathogens and Antimicrobial Resistance Unit.....	Elizabeth Bancroft, MD, SM
- Bioterrorism Preparedness and Response Unit	Raymond Aller, MD
- Vectorborne Diseases Unit	Rachel Civen, MD, MPH
- Varicella Surveillance Project.....	Teresa Maupin, RN, BS
- Food and Water Safety Unit.....	Roshan Reporter, MD, MPH
- Immunization Program	Alvin Nelson, MD, MPH
- Pediatric Spectrum of Disease Project	Toni Frederick, PhD, MSPH
- Pediatric HIV/AIDS Reporting Project.....	Getahun Aynalem
- Federal Epidemic Intelligence Service (EIS) Officer.....	Bhrett Lash, MD
Editor, Special Reports, 2001	Sadina Reynaldo, PhD

