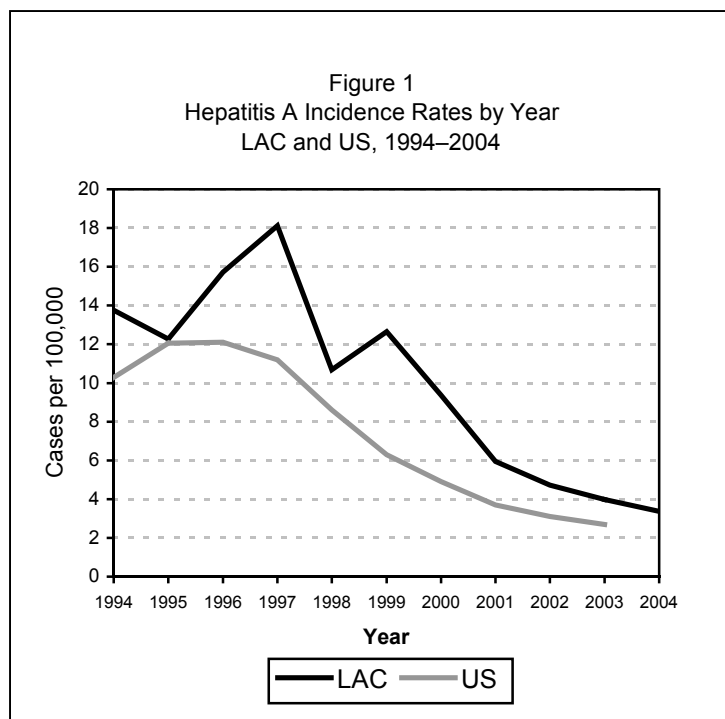




## HEPATITIS A INCREASE AND OUTBREAKS LOS ANGELES COUNTY, 2005

### BACKGROUND

In the US, hepatitis A has occurred in periodic epidemics approximately every decade, with the last epidemic occurring in 1995. Since then, rates of hepatitis A have plummeted with the introduction of an effective vaccine introduced in 1995 and with the 1999 recommendation by the Advisory Committee on Immunization Practices (ACIP) to provide universal childhood vaccination against hepatitis A in states (such as California) with the highest rates of the disease. In Los Angeles County (LAC), the last peak annual rate of acute hepatitis A occurred in 1997 (18 cases per 100,000 persons). In 2004, the number of reported cases declined 321 for an incidence of just 3 cases per 100,000 persons (Figure 1).



Prior to 2005, most reports of a positive test for hepatitis A IgM were considered by the LAC Department of Health Services (LACDHS) to represent acute cases of hepatitis A. This meant that persons without hepatitis symptoms and those with possibly false positive IgM tests were counted as cases of acute hepatitis A. But starting in 2005, LACDHS applied the CDC definition of acute hepatitis A to be consistent with the case definitions for acute hepatitis surveillance as published by the CDC and the Council of State and Territorial Epidemiologists (CSTE).<sup>1</sup> This change definition was enacted to ensure comparability of rates among jurisdictions and to better describe populations at risk for hepatitis A.

Using the new case definition from January-July, 2005, LACDHS received the same number of suspect reports of acute hepatitis A each month as in 2004—but the number of cases *confirmed*

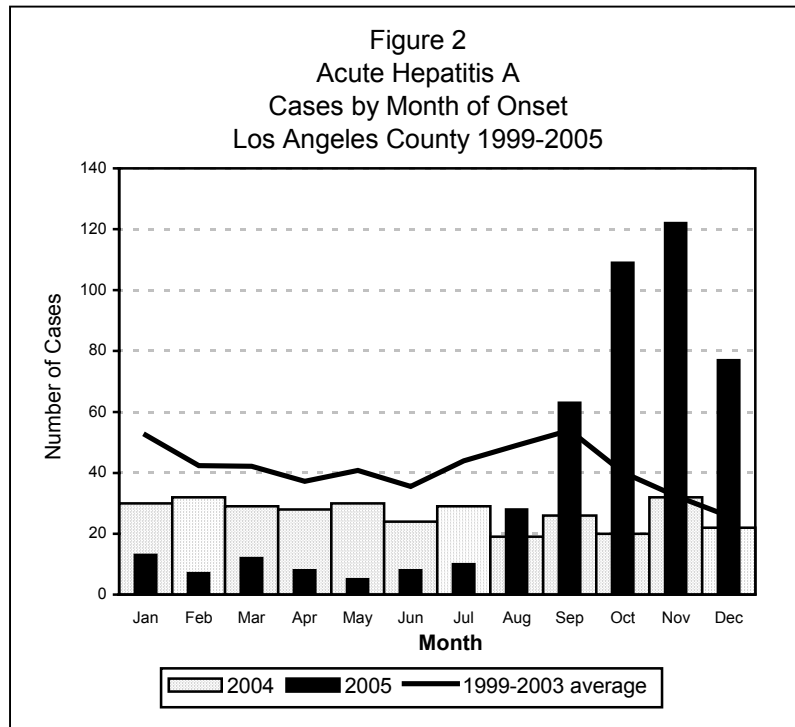
as acute dropped by 70% (Figure 2). However, starting in August 2005, there was a marked increase in the number of both reported and confirmed hepatitis A cases in LAC. By April 7, 2006, there were a total of 466 confirmed cases with onset in 2005 compared to just 321 in 2004. The increase in cases occurred in the latter half of 2005 when 403 confirmed cases with onset between August 1 to December 31 (the “outbreak period”) occurred, versus 119 cases in the same time period in 2004 (Figure 2). Several point source outbreaks were identified, and in particular, the downtown homeless population was recognized as being at increased risk for acquiring hepatitis A.

As a consequence, during the latter half of 2005, LACDHS enacted: multiple outbreak investigations, a general population case-control study, a detailed epidemiologic analysis of all reported cases,

<sup>1</sup> A case of hepatitis A is defined as a person with new clinical findings (i.e., onset date, jaundice, fever, fatigue, etc.) and with appropriate laboratory tests (e.g., hepatitis A IgM+, elevated liver function tests). Later during this investigation, acute cases patients were defined as those who were unable to be interviewed (primarily the homeless), but who had a positive test for HAV IgM and an alanine aminotransferase (ALT) level >300. If a reported case met either case definition, it was closed as “confirmed acute.” Otherwise, the report was closed as “false.”



environmental health investigations (including produce trace-backs), and serologic investigations in conjunction with the CDC for hepatitis A virus strain typing. These actions were taken in an effort to determine the cause(s) of the unexpected increase of acute hepatitis A.



Investigations were complicated by the long incubation period for hepatitis A (2-6 weeks) and the multiple means of acquiring hepatitis A (e.g., contaminated food or water, sex, drugs, travel to endemic countries, etc.). These factors made it especially difficult to link cases and to determine with accuracy a single point source for infection. Furthermore, during the course of our investigations, it was revealed that LACDHS's largest reporting agency had ceased reporting positive laboratory results for HAV IgM since October 2004 due to an error in computer programming after changing laboratory tests for acute hepatitis A. The test change resulted in two outcomes. First, test results were no longer automatically and

electronically reported to LACDHS (or any other Southern California county) for 13 months. Second, the percent of positive HAV IgM test results from this reporting source increased 5-fold. A large number of patients with a positive test for acute hepatitis A had no symptoms or other clinical criteria of hepatitis A. All positive test results (n=300) for the time period October 2004-October 2005 from this reporting source were transmitted to LACDHS on a single day in November 2005 for investigation and follow-up; this greatly increased the challenges in investigating the epidemiologic trends of hepatitis A in LAC.

The following is an overview of the distinct hepatitis A outbreaks and populations that were investigated.

1. Homeless, Downtown Los Angeles:

In October 2005, ACDC identified four cases of acute hepatitis A among volunteers and patrons of a homeless shelter in the downtown "skid row" area of Los Angeles. Since two cases occurred in volunteers who live with and prepare food for other volunteers of the shelter, all volunteers were offered Immune Globulin (IG) to prevent the acquisition of hepatitis A. The subsequent investigation did not confirm linkage between any cases and any homeless shelters. A total of 48 cases with some association with the homeless in downtown Los Angeles, with dates of onset or diagnosis between September-December 2005, were confirmed. The monthly number of confirmed cases in the homeless peaked in October (N=17)—which was prior to the peak in the general population. No baseline data of the prevalence of hepatitis A in the homeless prior to September 2005 exists, but local healthcare providers noted that cases of hepatitis A being treated were above "normal levels." Because of the multiple overlapping exposures to several soup kitchens, food sources, and shelters, and due to the inability to interview many homeless cases, no point source was identified. ACDC worked with the DHS homeless services coordinator to distribute hygiene and prevention messages to healthcare providers and homeless shelters in the downtown Los Angeles and across the county. Serum from a homeless patient was sent to CDC for hepatitis A viral sequencing.



2. Mexican Restaurant, Downtown Los Angeles:

A total of 17 cases of hepatitis A were confirmed in persons who ate at a downtown Mexican restaurant on September 14 or 15, 2005. A case-control study was not conducted because the link between the restaurant and cases was not identified until November, when many cases of acute hepatitis A with onset in October were re-interviewed with an extensive food history questionnaire. The LACDHS Food and Milk Program investigated the restaurant in November and found no food handling violations, no evidence that food handlers were ill in September or contemporaneously, and no produce suppliers that could be specifically linked to the other outbreaks in LAC during 2005. Food handlers were not tested for acute hepatitis A and no serum specimens from the cases were available for viral sequencing.

3. Workplace Setting, San Gabriel Valley:

In November of 2005, ACDC investigated an outbreak of 19 people with acute hepatitis A who had all eaten at a movie set on October 3, 2005. A case-control study was enacted to determine risk factors for illness. A case was defined as a person who ate at the worksite on October 3, 2005 and who was IgM positive and symptomatic. Controls were those that ate at the worksite on the same day, but were well and did not have any of the following exclusion characteristics: clinical symptoms of hepatitis A, past diagnosis or vaccination for hepatitis A, or a history of receiving immune globulin in the preceding 3 months. Food-handlers were tested for hepatitis A IgM and IgG; all tested negative.

Ultimately, 116 of the 246 people (47%) who were on the set that day were contacted—40 met the exclusion criteria, 18 cases and 58 controls were identified (one additional case was identified after the case-control study was concluded). After interviewing cases and controls, a stratified analysis suggested that of the 65 food items provided, only the following accounted for more than half the cases:

- the salad bar stratifying by the jerk chicken (OR=5.3, 95%CI: 1.08-26.24),
- the mixed greens stratifying by the jerk chicken (OR= 5.06, 95%CI: 1.52-16.84),
- the jerk chicken stratifying by the salad bar (OR=4.06, 95%CI 1.26-13.15),
- and the jerk chicken stratifying by the mixed greens (OR=4.65 95%CI 1.39-15.48).

Since the jerk chicken had no raw ingredients, lettuce (pre-washed mixed baby greens) was implicated as the most likely cause of this outbreak. A trace-back performed by the LACDHS Food and Milk Program revealed that the caterer purchased the lettuce from a produce vendor who bought the lettuce from *another* vendor who bought ultimately bought it from a farm outside of LAC. LACDHS was unable to determine where, and if, the contamination of the lettuce occurred between the farm and the movie set. Given that no other outbreak implicated that farm or the other two lettuce vendors, a detailed trace-back and investigation of these food purveyors was not conducted. No sera were collected from cases in this outbreak.

4. Café, Downtown Los Angeles:

Between November 29 and December 7, five employees of a downtown restaurant were diagnosed with acute hepatitis A—four of them, including a cook, worked while ill. Because several food-handlers worked while symptomatic, a public announcement was made and IG was provided at no cost to the public (>650 doses) and to the other employees at the restaurant (50 doses).

Serum specimens for hepatitis A IgM were collected from the other employees (n=51); none positive; no new employee cases were identified. Employees that had left this employment prior to the discovery of the outbreak also were contacted. At this restaurant, employees were served a “family style” meal before each shift. As the five employees diagnosed with hepatitis A had worked multiple overlapping shifts in the 2-6 weeks before they became ill, it was impossible to determine the source of illness. A cohort study of food preferences of restaurant employees was performed, but no individual food item that could account for the cases was identified. In addition, no cases among patrons were definitively linked to eating at this restaurant. There were no commonalities between the produce suppliers for this restaurant and those for the other restaurant and movie set and no other ill employees were identified, which eliminated the likelihood that another employee was the originating



source of infection. Sera were collected from the employee cases and from an additional case (who ate at this restaurant) were sent to CDC for strain typing.

5. Group Home, Antelope Valley:

Two confirmed cases of hepatitis A infection were identified at a substance abuse treatment facility in the Antelope Valley. Onset of jaundice occurred between December 6 and 10, 2005. Both cases lived in the facility during their entire incubation periods. Approximately 22 other residents complained of nausea/vomiting, diarrhea, muscle aches, and fever starting on November 24. A total of 33 residents, including the 22 ill residents, were tested and all were negative for acute hepatitis A. No common source was identified for the two cases and all other members of the treatment facility were offered IG to prevent acquisition of hepatitis A. Sera from both patients was sent to CDC for strain typing. No additional cases occurred.

## RESULTS

General Population Case-Control Study: Because of the generalized increase in hepatitis A throughout LAC, ACDC conducted a matched case-control study of confirmed hepatitis A cases with onset in October that were not part of any identified cluster or outbreak. Controls were identified through random digit dialing; telephone numbers were generated in stepwise progression (either up or down) from the matched case's phone number. In total, 21 cases and 42 matched controls were interviewed. Univariate matched analysis resulted in the following significant odds ratios (OR):

- bagged salad (OR 4.5, p value .013, 67% of cases exposed),
- spring mix bagged salad (OR 8.0, p value .0041, 43% of cases exposed),
- eating downtown (OR 5.5, p value .0025, 62% of cases exposed), and
- being currently employed (OR 2.8, p value .07, 86% of cases exposed).

Conditional logistic regressions using multiple models were subsequently used to examine which of the risk factors remained significant in the presence of other risk factors. Eating downtown remained strongly associated with illness (OR range 3.5 to 4.1 with all models being significant) and spring mix bagged salad remained slightly associated (OR range 3.1 to 4.2 with some models being marginally significant and others not being significant). Produce such as cilantro and green onions—which have been implicated in previous hepatitis A outbreaks—showed a significant protective effect. The results suggested that eating downtown was the most probable risk associated with acquiring hepatitis A. Although no sera was sent to CDC for sequencing from the October general population cases, sera was sent from November cases.

Environmental Health Inspections: The Environmental Health Food and Milk Program performed inspections of several food service purveyors in the investigation of the discrete outbreaks. This included restaurants (n=2), soup kitchens (n=7), produce vendors (n=2), and a catering truck. Their investigations included assessing employee health, hygiene conditions, produce suppliers and sources, opportunities for cross contamination. There was no evidence that the outbreaks of acute hepatitis A were associated with any personnel, common produce supplier, or poor food handling techniques.

Hepatitis A Virus Strain Typing: A total of 68 blood samples from LAC residents were sent to the CDC for viral strain typing. Of these, 40 tested positive for the presence of hepatitis A virus nucleic acid by PCR; 80% of these samples (n=32) were found to be a unique strain, not previously identified in North America. Samples from cases associated with the downtown restaurant, the homeless, and the group home (Antelope Valley) cluster matched the unique strain.

Epidemiologic Analysis of Confirmed Cases: Comparing the first seven months of 2005 (baseline period, January to July 2005) against the last five months of 2005 (outbreak period, August to December 2005), some differences appear (Table 1). First, outbreak cases were slightly older (mean age 38 years versus 34 years) and more likely to be within the age group for working age adults—82% of the outbreak cases occurred in adults aged 21-64 versus 64% of the cases during the baseline period. The gender ratio also skewed toward males; by the end of 2005, 64% of the cases occurred in men versus 57% during the



baseline period, and only 50% in 2004. Another notable finding was that the proportion of cases that were Black increased from 4 to 14% during the outbreak period.

The overall increase in hepatitis A cases was widespread throughout LAC—all health districts reported an increase during the outbreak period as compared to the same time period in the previous year, 2004. But despite the widespread increase, a notable cluster occurred—16% of the cases during the outbreak period were reported from the Central Health District compared to just 3% of the cases during the same time period in 2004.

<b>Table 1. Comparison of Confirmed Hepatitis A Case Characteristics Before (January–July) and During (August–December) the Outbreak Period Los Angeles County, 2005</b>			
<b>Characteristics</b>	<b>Time Period</b>		
	<b>January–July (N=392)</b>		<b>August–December (N=63)</b>
<b>Age in Years</b>			
Mean	34		38
Median	33		37
Range	1-89		1-86
<b>Age Category</b>	<b>n</b>	<b>(%)</b>	<b>n (%)</b>
<1	0	(0)	0 (0)
1-4	2	(3)	5 (1)
5-14	8	(13)	17 (4)
15-20	7	(11)	27 (7)
21-34	22	(35)	128 (33)
35-44	8	(13)	77 (20)
45-54	8	(13)	77 (20)
55-64	2	(3)	39 (0)
≥65	7	(11)	22 (6)
<b>Gender</b>	<b>n<sup>1</sup></b>	<b>(%)</b>	<b>n (%)</b>
Male	36	(57)	249 (64)
Female	27	(43)	162 (36)
<b>Race/Ethnicity</b>	<b>n<sup>2</sup></b>	<b>(%)</b>	<b>n<sup>3</sup> (%)</b>
Asian	7	(13)	30 (9)
Black	2	(4)	44 (14)
Latino	21	(38)	102 (32)
White	26	(46)	143 (45)

1 N=391

2 N=319

3 N=56

## DISCUSSION

The clusters of illness identified in two downtown restaurants, the homeless in downtown, and the results of the general population case control study suggest that the most likely source of infection may have originated in downtown Los Angeles. While the caterer from the workplace outbreak, the homeless



shelter, both restaurants, and the group home all received some produce from distributors located in downtown Los Angeles, no further commonalities could be identified. Furthermore, produce that is most likely associated with hepatitis A outbreaks—green onions and cilantro—was not implicated in any of the outbreaks or in the general population. Additionally, the general population case control study actually showed a protective effect for both food items.

Consequently, the source of the outbreaks remains questionable. It is possible that this new hepatitis A strain was introduced to the community in August, spread at modest levels that month and in September, and reached a critical mass in October and November. It is clear that the distribution of the strain was widespread in that 80% of the samples had the same strain type and this strain. It is possible that this particular strain may be more infectious than others previously seen in Los Angeles, but the comparative virulence of this strain is unknown. In other communities, outbreaks have been sustained by, often asymptomatic, transmission of the virus between children and to adults. However, since there was no increase in the percentage of cases seen in children or in the percentage of cases with a connection to a school or daycare, this source of transmission is not likely.

The number of reported and confirmed cases decreased each month since November (Figure 2) and no further discrete outbreaks were reported. Despite the decrease in cases since December 2005, the number of reported cases in March 2006 was still double that at the same time in 2005 (the “baseline period”). Accordingly, ACDC continued to monitor the situation.