

# Sources of Infection Among Persons With Acute Hepatitis A and No Identified Risk Factors During a Sustained Community-Wide Outbreak

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**ABSTRACT.** *Context.* Hepatitis A is a common vaccine-preventable disease in the United States. Most cases occur during community-wide outbreaks, which can be difficult to control. Many case-patients have no identified source.

*Objective.* To identify foodborne and household sources of hepatitis A during a community-wide outbreak.

*Design.* Serologic and descriptive survey.

*Setting.* Salt Lake County, Utah.

*Participants.* A total of 355 household contacts of 170 persons reported with hepatitis A during May 1996 to December 1996, who had no identified source of infection; and 730 food handlers working in establishments where case-patients had eaten.

*Main Outcome Measure.* Prevalence of immunoglobulin M antibodies to hepatitis A virus (IgM anti-HAV) among household and food service contacts.

*Results.* Overall, 70 household contacts (20%) were IgM anti-HAV-positive, including 52% of children 3 to 5 years old and 30% of children <3 years old. In multivariate analysis, the presence of a child <3 years old (odds ratio [OR]: 8.8; 95% confidence limit [CL]: 2.1,36) and a delay of  $\geq 14$  days between illness onset and reporting (OR: 7.9; 95% CL: 1.7,38) were associated with household transmission. Of 18 clusters of infections linked by transmission between households, 13 (72%) involved unrecognized infection among children <6 years old. No food handlers were IgM anti-HAV-positive.

*Conclusion.* During a community-wide outbreak, HAV infection among children was common, was frequently unrecognized, and may have been an important source of transmission within and between households. Transmission from commercial food establishments was uncommon. Ongoing vaccination of children may prevent future outbreaks. *Pediatrics* 2000;106(4). URL: <http://www.pediatrics.org/cgi/content/full/106/4/e54>; *hepatitis A, epidemiology, outbreak, prevention and control, immunization*.

ABBREVIATIONS. IG, immune globulin; HAV, hepatitis A virus; SLCCHD, Salt Lake City-County Health Department; IgM anti-HAV, immunoglobulin M antibodies to hepatitis A virus; CDC, Centers for Disease Control and Prevention; RR, risk ratio; CL, confidence limits; OR, odds ratio.

Hepatitis A is a commonly reported vaccine preventable disease in the United States. In 1996, over 31 000 cases were reported and an estimated 150 000 infections occurred.<sup>1</sup> Among reported cases, the most frequently reported source for infection is household or sexual contact with a person with hepatitis A, accounting for 22% to 26% of cases.<sup>2,3</sup> Other recognized potential risk factors include male homosexual preference, illicit drug use, international travel, and association with child care settings experiencing an outbreak.<sup>4-12</sup> Foodborne outbreaks are recognized infrequently and account for <10% of reported cases.<sup>3,12</sup> A source for infection cannot be identified for 40% to 50% of reported cases.<sup>3,12</sup>

Most cases of hepatitis A occur during community-wide outbreaks, during which the highest rates of disease are reported among children, adolescents, and young adults.<sup>2</sup> These outbreaks have been difficult to control, despite implementation of preventive measures and postexposure prophylaxis with immune globulin (IG). Recently-licensed safe and effective hepatitis A vaccines offer new opportunities for prevention.<sup>13,14</sup>

Salt Lake County, Utah, has experienced sustained community-wide outbreaks of hepatitis A approximately every 8 years. Salt Lake County (population: ~800 000 persons) includes Salt Lake City, the state's most urban area, and its surrounding suburban and rural communities. During the most recent outbreak between 1992 and 1996, an average of 473 cases were reported each year. This annual incidence of 65 cases per 100 000 population is ~6 times higher than the national rate.<sup>1</sup> Similar to the pattern reported in other communities in the United States that experience community-wide outbreaks, less than one half of all reported cases had a recognized source for infection.<sup>5,6,11,12,15-17</sup>

To design effective prevention strategies, a better understanding of the sources of infection and modes of transmission of hepatitis A virus (HAV) in communities is needed. Thus, we undertook an intensive investigation of all reported hepatitis A cases with no identified sources for infection to explore the extent

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to which these persons might have acquired hepatitis A from unrecognized foodborne transmission from infected food handlers or person-to-person transmission within and between households. The findings of the investigation have ramifications for control strategies, particularly use of hepatitis A vaccine.

## METHODS

### Case Investigation

Between May 31, 1996 and December 3, 1996, 2 Salt Lake City-County Health Department (SLCCHD) nurses investigated all serologically confirmed hepatitis A cases reported among residents of Salt Lake County. A nurse interviewed the ill person or his/her guardian using a standard questionnaire; evaluated potential sources for infection; identified household, sexual, social, and child care contacts; elicited a detailed history of the food establishments patronized by the ill person during their exposure period (2–6 weeks before their onset of illness); and implemented routine control measures.<sup>2,18</sup> Cases with recognized potential sources for infection identified during this initial investigation—including close contact with a person with hepatitis A, international travel, consumption of raw shellfish, illicit drug use, and homosexual or bisexual activity—were not investigated further. Persons who were homeless, unable to be interviewed, or had been incarcerated within 50 days of the onset of their illness were also excluded from further study. For the remaining case-patients, we conducted an intensive investigation to determine whether infection could have been acquired from exposure to household contacts or food handlers in commercial settings with unrecognized HAV infection.

### Household Contacts

Household contacts were defined as persons who, during the exposure period: 1) lived in the residence; or 2) spent at least 20 hours per week at the residence; or 3) were children regularly cared for in the residence for at least 10 hours per week. After giving informed consent, household contacts had blood drawn for hepatitis A serologic testing and completed a questionnaire concerning their demographic characteristics and history of exposure to HAV, vaccine, IG, and child care settings. Household contacts who had immunoglobulin M antibodies to HAV (IgM anti-HAV) were reinterviewed to determine the presence and onset of symptoms.

### Transmission

To evaluate transmission patterns and assess risk factors for transmission within and between households, dates of onset of symptoms were used to determine whether 2 infected persons were coinfecting (ie, the dates were 14 or fewer days apart), or whether 1 or more generations of transmission had occurred (ie, the dates were 15–50 or >50 days apart, respectively). Household transmission was considered to have occurred if: 1) at least 1 symptomatic IgM anti-HAV-positive person (other than the index case) was identified; and 2) symptom onset dates indicated that at least 1 generation of HAV transmission occurred. Households where no transmission occurred were defined as those in which: 1) at least 1 anti-HAV-negative person was identified; 2) any IgM anti-HAV-positive person identified was determined to be coinfecting with the index case; and 3) the serologic status of all household members was determined. Only households in which the presence or absence of transmission could be confirmed were included in the analysis of within-household transmission.

Transmission between households was assessed by documenting the timing, location, and type of contact between HAV-infected persons identified by public health authorities or serologic testing.

### Food Service Establishments and Food Handlers

Food handlers at food service establishments from which at least 2 unrelated case-patients had obtained food during their exposure period and within 6 weeks of each other were invited to participate. After giving consent, the food handler had blood drawn for HAV serologic testing and completed a questionnaire to determine demographic characteristics and history of exposure to

HAV, vaccine, or IG. In addition, the establishment underwent a systematic inspection by a SLCCHD environmental health inspector, including observation of food handling and hand-washing practices and inspection of the food preparation, storage, and sanitation facilities.

### Laboratory Methods

Serum was analyzed by the Hepatitis Reference Laboratory, Centers for Disease Control and Prevention (CDC) for total and IgM anti-HAV using standard assays (HAVAB, HAVAB-M, Abbott Laboratories, Abbott Park, Chicago, IL).

### Institutional Review Board

The study protocol was approved by the institutional review boards of the CDC and the University of Utah Health Sciences Center. Study participants or their parents/guardians were notified of their serologic test results.

### Statistical Methods

Epi-Info and Logistic software were used to manage and analyze the data.<sup>19,20</sup> Risk ratios (RRs) and prevalence ratios, Taylor series 95% confidence limits (CLs), and Yates corrected *P* values were used to measure associations between recent or past infection and exposures of interest and among age, reporting, and symptoms. Odds ratios (ORs), Fisher's exact 95% CLs, and Yates corrected or Fisher's exact *P* values were used to evaluate factors associated with household transmission. Factors associated with household transmission were further evaluated with multivariate modeling using backward elimination techniques. Variables associated with household transmission in the univariate analysis with *P* values <.1 were included in the initial model and eliminated sequentially using the log-likelihood statistic.

## RESULTS

### Findings From Routine Surveillance

During the 6-month study, 393 hepatitis A cases were reported to the SLCCHD. Thirty-three persons (8%) were hospitalized and 2 (.5%) died, both of whom had underlying chronic liver disease. Incidence rates were higher among males compared with females, and among persons of Hispanic ethnicity compared with persons of white race and non-Hispanic ethnicity (Table 1).

A total of 61 case-patients (15%) were excluded from further study because we were unable to interview the case-patient (*n* = 35) or because no potential source for infection was identified and the case-patient reported recent incarceration (*n* = 9), homelessness (*n* = 16), or having been outside Salt Lake County for the entire exposure period (*n* = 1). Of the remaining 332 case-patients (85%), 162 (49%) reported potential sources for infection, including: contact with a confirmed or suspected case (*n* = 60), international travel (*n* = 5), homosexual or bisexual activity (*n* = 20), illegal drug use (*n* = 99), and eating raw shellfish (*n* = 5; Table 2). The remaining 170 case-patients (51%) were selected for further investigation.

### Investigation of Household Exposures

#### *Serologic Testing of Household Contacts*

A total of 355 of 476 household contacts (75%) living in 108 of the 138 households (78%) with more than 1 person underwent serologic testing. The proportion of household members for which serologic testing was obtained ranged from 60% among children <3 years of age to 86% among adults 45 years or older.

**TABLE 1.** Demographic Characteristics of Persons Reported With Hepatitis A: May 31, 1996 Through December 3, 1996, Salt Lake County, Utah ( $n = 393$ )

	All Persons Reported With Hepatitis A $n$ (%)	Incidence Rate (per 100 000) <sup>†</sup>	Case-Persons Selected for Further Study $n$ (%)
Gender	393 (100)	96	170 (100)
Male	235 (60)	115	82 (48)
Female	158 (40)	77	88 (52)
Racial/ethnic group			
White, non-Hispanic	285 (81)	79	149 (88)
Hispanic	47 (13)	150	17 (10)
Asian/Pacific Islander	4 (1)	‡	2 (1.1)
Black, non-Hispanic	7 (2)	‡	1 (<1)
Native American	5 (1)	‡	0 (0)
Not reported	45 (*)	‡	1 (<1)
Age group, y			
<5	10 (2)	26	5 (3)
5-14	81 (21)	110	51 (30)
15-29	128 (32)	128	48 (28)
30-44	129 (33)	136	44 (26)
>44	45 (12)	45	22 (13)

\* Excluded persons for whom race/ethnicity data were not reported when calculating percentages.  
<sup>†</sup> Annualized, based on US Census Bureau 1996 population estimates and Utah State Governor's Office of Planning and Budget, Utah Population Estimates Committee, 1997 economic and demographic projections.  
<sup>‡</sup> Rates not calculated. Numerator too small.

**TABLE 2.** Identified Risk Factors of Hepatitis A Cases, Before and After Intensive Investigation: May 31, 1996 Through December 3, 1996, Salt Lake County, Utah ( $n = 332$ )

Reported Risk Factors*	Before Intensive Investigation $n$ (%)	After Intensive Investigation $n$ (%)
Close contact with a confirmed or suspect case	60 (18)	93 (28)
International travel	5 (2)	5 (2)
Homosexual or bisexual activity	20 (6)	20 (6)
Consumption of raw shellfish	5 (2)	5 (2)
Illegal drug use	99 (30)	100 (30)
Exposure to infected food handler	0 (0)	3 (<1)
School outbreak	0 (0)	10 (3)
Attend or employed in a child care setting	23 (7)	23 (7)
Household contact attends or is employed in a child care setting	42 (13)	33 (10)
No identified risk factors	132 (40)	106 (32)

\* Reported during the exposure period. Categories are not mutually exclusive.

A total of 70 household contacts (20%) were IgM anti-HAV-positive, indicating recent or acute infection, 227 (64%) were total anti-HAV-negative (ie, susceptible), and 58 (16%) were total anti-HAV-positive and IgM anti-HAV-negative, indicating past infection and immunity (Fig 1). The highest proportion of IgM anti-HAV-positive persons occurred among children 3 to 5 years old (52%), followed by children <3 years old (30%), and 6 to 14 years old (24%; Fig 1).

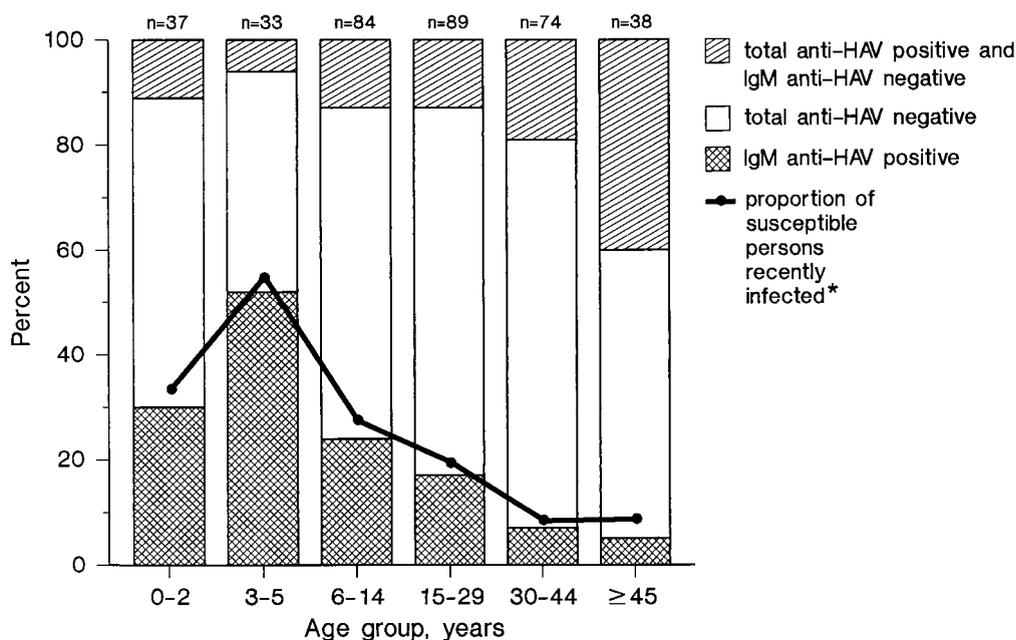
Among children (case-patients and household contacts) <6 years old, those who attended child care were no more likely to be IgM anti-HAV-positive than were those who did not (14/23 [61%] vs 28/55 [51%], respectively; RR: 1.2; 95% CL: .8-1.8).

#### Transmission Within Households

Of the 47 households (44%) that included at least 2 IgM anti-HAV-positive persons (range: 2-8), household transmission could be confirmed in 20 (43%).

The absence of household transmission could be confirmed in 41 households (38%). Thus, a total of 61 households (56%) were included in the analysis of factors associated with household transmission. In the remaining households, factors associated with household transmission could not be assessed, primarily because not all household members were tested ( $n = 23$ ), the date of infection among IgM anti-HAV-positive asymptomatic persons could not be ascertained ( $n = 18$ ), or all contacts were already immune ( $n = 6$ ). Among the households that included children under 6 years of age, the percentage of households in which the occurrence or absence of transmission could be determined (54%) and could not be determined (57%) was similar.

In univariate analysis, transmission within households was associated with having a child <3 years of age in the household, a child 3 to 5 years of age in the household, and a delay of 14 or more days between



\* Number IgM anti-HAV positive / Number IgM anti-HAV positive or total anti-HAV negative

**Fig 1.** Distribution of hepatitis A serologic markers among household contacts of persons with hepatitis A and no identified source of infection ( $n = 355$ ).

**TABLE 3.** Association Between Selected Factors and Household Transmission of Hepatitis A: Salt Lake County, Utah, 1996 ( $n = 61$ )

Factor	Households With Transmission ( $n = 20$ )	Households With No Transmission ( $n = 41$ )	OR (95% CL)	<i>P</i> Value
Child under 6 y of age resides or is regularly cared for in the household	16 (80%)	17 (42%)	5.6 (1.4, 26.6)	.01
Child 3–5 y of age resides or is regularly cared for in the household	12 (60%)	11 (27%)	4.1 (1.1, 15.1)	.03
Child under 3 y of age resides or is regularly cared for in the household	13 (68%)	11 (27%)	5.1 (1.4, 19.2)	.01
Delay between onset and report date of the index case ( $\geq 14$ d)	8 (40%)	6 (15%)	3.9 (.95, 16.5)	.05*
Household member under 6 y of age attends a grouped child care setting for 4 or more h per wk	6 (30%)	8 (20%)	1.8 (.4, 7.1)	.52
Household size >5 persons	9 (45%)	12 (29%)	2.0 (.6, 7.1)	.35

\* Fisher's exact *P* value used because expected value in 1 cell <5.

illness onset in the index case and reporting to the health department (Table 3). In multivariate analysis, having a child under 3 years of age in the household (OR: 8.8; 95% CL: 2.1,36;  $P = .002$ ) and a delay of 14 or more days between illness onset in the index case and reporting (OR: 7.9; 95% CL: 1.7,38;  $P = .009$ ) were the only factors associated with household transmission.

#### Transmission Between Households

We documented 18 clusters of infections that involved >1 household and >1 generation of infection. A median of 3 households (range: 2–14) and 5 documented infections (range: 2–24) were involved with each cluster. Exposures resulting in transmission included household-like contact such as baby-sitting or visiting relatives or close neighbors. Thirteen clusters (72%) were associated with unrecognized infection among children <6 years old, including 4 clusters involving family child care settings where the rec-

ommended control measures were not fully implemented.<sup>2</sup> The remaining 5 clusters involved transmission among older children and adults with sexual or household-like exposure to one another. The largest cluster involved 6 generations of transmission and 24 documented infections among residents of Salt Lake County, California, and Idaho (Fig 2).

#### Investigation of Commercial Food Handlers

Eighty-three commercial food establishments that employ ~4000 food handlers were named by 2 or more unrelated case-patients. A total of 32 of these establishments (39%) participated, including 8 of 9 establishments named by 4 or more unrelated persons, and 3 of 4 establishments with a food handler already reported with hepatitis A. The establishments that participated and those that did not were similar with respect to the type of establishment, volume of customers, and the proportion in which

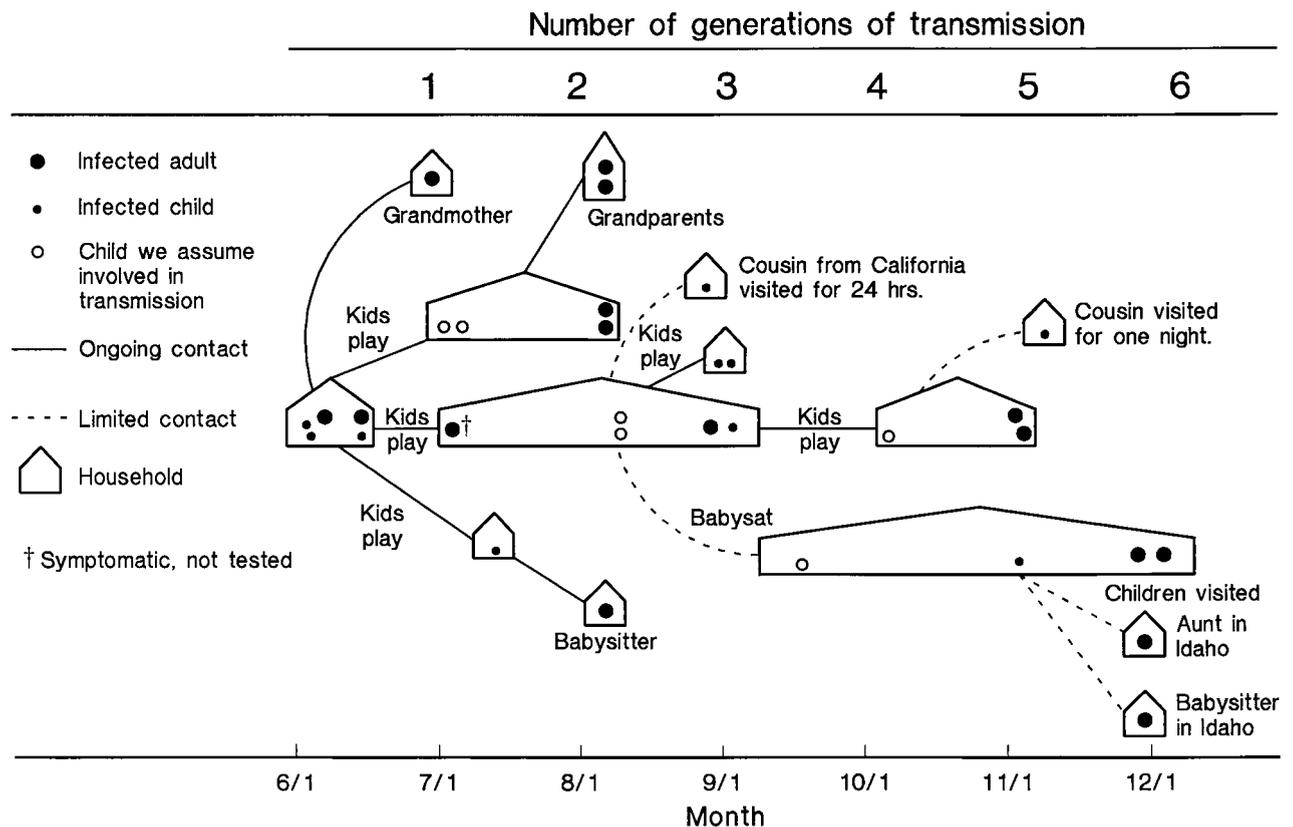


Fig 2. Relationship between households associated with 1 cluster of hepatitis A in Salt Lake County, Utah, from June through December 1996.

food handlers were observed using poor food handling practices (78% vs 61%, respectively).

Serologic results were available for 730 food handlers (40%), including 713 current (48%) and 17 former employees (5%). None of the tested food handlers were IgM anti-HAV-positive. None of the untested food handlers reported jaundice.

Past infection was documented in 253 food handlers (35%) and was significantly more prevalent among food handlers born in Mexico (140/143 [98%]) and South America (19/22 [86%]), compared with those born in the United States (69/512 [13%]; prevalence ratios: 7.3, 6.4, respectively;  $P < .0001$ ).

### Routine Versus Intensive Investigation

#### Characteristics of IgM anti-HAV-Positive Persons

A total of 240 IgM anti-HAV-positive persons were identified from routine reports to the health department (71%) and by intensive investigation of their household contacts (29%). The vast majority (223; 93%) reported symptoms; 169 (70%) were jaundiced. However, only 11 of the 34 symptomatic children <6 years old (32%) were jaundiced. Symptoms reported by nonicteric, symptomatic adults and children included fever (65%), abdominal pain (61%), vomiting (65%), and fatigue (56%).

#### Reporting of Cases to the Health Department

Reporting was associated with the presence of jaundice, both among young children and older children and adults. Only 35% of the symptomatic non-icteric cases (19/54) were reported, compared with

89% of the jaundiced case-patients (151/169; RR: 2.5; 95% CL: 1.8,3.7). After controlling for the presence of jaundice using stratified analysis, age was not associated with reporting (data not shown). However, because of the relative infrequency of jaundice among young children, only 41% of cases among children <6 years old were reported. In comparison, 83% of the cases among older children and adults were reported.

#### Sources of Infection After Intensive Investigation

Through intensive investigation, the probable source of infection for 33 additional case-patients was determined to involve household (55%) or household-like (45%) contact with an infected person. Therefore, among the 332 case-patients reported and investigated during the study, a total of 93 (28%) reported contact with an infected person during their exposure period (Table 2). Three case-patients (<1%) reported eating at an establishment that had a food handler reported with hepatitis A at the time the exposure occurred; other potential sources were identified for an additional 11 case-patients (3%; Table 2).

Child care-related exposures were initially reported by 51 of the 332 case-patients (15%) reported and investigated during the study, including 23 (7%) who attended or worked in child care and 42 (13%) who had a household member that attended or worked in child care. However, more likely sources unrelated to child care were identified for 16 case-patients, and all the child care-attending household

contacts for 8 case-patients were anti-HAV-negative and were excluded as the source of infection. Thus, exposures associated with child care could have been the source of infection for only 27 of the case-patients (8%) reported and investigated during the study.

In total, after routine and intensive investigation, a possible source of infection was identified for 226 of the reported case-patients (68%; Table 2). Even after intensive investigation, a source of infection could not be identified for the remaining 106 case-patients (32%; Table 2). The demographic characteristics of these case-patients were similar to those of all case-patients who underwent intensive investigation (data not shown).

## DISCUSSION

In the United States, most hepatitis A occurs during community-wide outbreaks in which many hepatitis A cases do not have an identified source for infection. It has been hypothesized that some of these persons acquire their infection through person-to-person transmission, particularly from children with asymptomatic infection.<sup>11,12,17</sup> The findings of this study indicate that person-to-person transmission, both within and between households, occurred frequently, often involving young children with unrecognized HAV infection. Although there is often a public perception that many hepatitis A cases occur from foodborne sources, we found no evidence of unrecognized HAV infection among food handlers in commercial food establishments, and foodborne transmission from recognized infected food handlers was extremely uncommon during this community-wide outbreak.

In households of persons reported with hepatitis A with no identified source, HAV infection among young children was common and frequently undetected. Nearly one half of household contacts under 6 years of age who underwent serologic testing were found to be IgM anti-HAV-positive. Although asymptomatic infection was unusual, the symptoms of infected children were nonspecific and, in most cases, not recognized as hepatitis A.

These HAV-infected children were frequently the source of infection for others. The presence of children <3 years of age was associated with transmission within the household, consistent with reports that implicate diapered children as the most important vectors of HAV transmission in child care centers.<sup>9</sup> Although not associated with household transmission in multivariate analysis, one half of all the 3- to 5-year-old children tested were IgM anti-HAV-positive, and many were previously-unrecognized links in clusters of transmission between households.

Few nonicteric cases were diagnosed and reported to the health department. Thus, the number of reported cases underestimated the true number of symptomatic hepatitis A cases and of HAV infections, as has been previously noted.<sup>1,2</sup> Because children were less likely to have jaundice, they were disproportionately underreported; only 41% of symptomatic cases among children <6 years of age were identified.

Attendance at a child care center or household

contact with someone who attends child care has traditionally been considered a risk factor for hepatitis A.<sup>2,6,9,11</sup> In our study, although children were frequently infected, most transmission occurred within and between households. We found no evidence that attendance in child care increased the risk of acquiring HAV infection. As we demonstrate, without serologic testing of the household contacts, risk factor information derived from surveillance data may overestimate the importance of exposure to child care settings and underestimate the importance of infected household contacts as a source of hepatitis A.<sup>3,12</sup>

Serologic testing of over 700 food handlers identified none with recent infection, and intensive investigation of reported cases identified only 3 persons who might have acquired their infection from previously-reported infected food handlers. Thus, foodborne transmission from infected food handlers did not constitute an important unrecognized source of hepatitis A. These findings support surveillance data indicating that infected food handlers are a relatively uncommon source of hepatitis A in the United States.<sup>3</sup>

This study has limitations primarily related to its descriptive nature. We performed serologic testing on 75% of the eligible household contacts and cannot determine how the serologic status of the untested persons might have influenced the results of our investigation. In addition, we were unable to determine who transmitted to whom within a number of households. Nevertheless, we were able to document whether transmission occurred in the majority of participating households without selectively excluding households with young children, where the direction of transmission might have been difficult to determine because of asymptomatic infections. With respect to the investigation of food handlers, over one half of the food establishments named by case-patients declined to allow their employees to be tested. However, the establishments that participated were similar to those that did not, and it is unlikely that we failed to detect a significant number of infected food handlers. Finally, the epidemiology of hepatitis A in the United States is heterogeneous, and the study's findings may not be generalizable to all communities that experience hepatitis A outbreaks. The demographic characteristics of the population of Salt Lake County differ slightly from national figures, with a lower median age, higher median income, and larger household size. Nonetheless, the pattern we describe in Salt Lake County is similar to that observed in other communities during community-wide outbreaks.<sup>12,15,17</sup>

The study's findings support the conclusion of the Advisory Committee on Immunization Practices that widespread ongoing vaccination of young children will be necessary to prevent community-wide outbreaks and to effect significant and sustained reductions in hepatitis A incidence.<sup>2</sup> Even after the intensive investigations conducted during this study, a probable source for infection could not be identified for 32% of persons reported with hepatitis A during the study, underscoring the inherent limitations of

vaccination programs targeted to persons reporting recognized risk factors. Young children frequently served as the source for infection for older children and adults, suggesting that vaccination of young children might also decrease disease incidence among older age groups. Because of these considerations, the health department began a campaign to vaccinate ~4000 children 2 to 6 years of age living in 1 geographic region of Salt Lake County with the highest reported rate of hepatitis A and to continue vaccinating subsequent cohorts of young children.

Recently, the Advisory Committee on Immunization Practices expanded its recommendations for routine hepatitis A vaccination of children to include areas of the country with consistently elevated hepatitis A rates, such as Salt Lake County.<sup>2</sup> Over time, routine vaccination of successive cohorts of young children in these areas, and ultimately of young children nationwide, should result in a sustained reduction in hepatitis A incidence in the United States.

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## **Sources of Infection Among Persons With Acute Hepatitis A and No Identified Risk Factors During a Sustained Community-Wide Outbreak**

Catherine Janes Staes, Thomas L. Schlenker, Ilene Risk, Kyle G. Cannon, Heath Harris, Andrew T. Pavia, Craig N. Shapiro and Beth P. Bell

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