

Hepatitis A in Hispanic Children Who Live Along the United States–Mexico Border: The Role of International Travel and Food-Borne Exposures

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ABSTRACT. *Objectives.* Hispanic children who live along the United States–Mexico border historically have had among the highest hepatitis A rates in the United States, but risk factors have not been well characterized. The objective of this study was to examine risk factors associated with acute hepatitis A virus (HAV) infection in Hispanic children who live along the United States–Mexico border in San Diego County, California.

Methods. In this case-control study, hepatitis A cases among Hispanic children who were younger than 18 years reported from June 1998 through August 2000 were matched by age group and exposure period to Hispanic children who were susceptible to HAV infection. Participants and their families were interviewed about demographic information and potential sources of HAV infection, including attending child care, food and waterborne exposures, cross-border and other international travel, and travel-related activities.

Results. Participants included 132 children with hepatitis A and 354 control subjects. The median age of study participants was 7 years (range: 1–17). Sixty-seven percent of case-patients traveled outside the United States during the incubation period, compared with 25% of the children without hepatitis A (odds ratio [OR]: 6.3; 95% confidence interval [CI]: 4.0–9.7); all children, except 1, had traveled to Mexico. In multivariate analysis, hepatitis A was associated with having eaten food from a taco stand or street food vendor (adjusted OR: 17.0; 95% CI: 4.1–71.1) and having eaten salad/lettuce (adjusted OR: 5.2; 95% CI: 1.3–20.1) during travel.

Conclusions. Hepatitis A among Hispanic children who live in an urban area of the United States–Mexico border is associated with cross-border travel to Mexico and food-borne exposures during travel. Travelers to areas where hepatitis A is endemic should receive hepatitis A vaccine before travel. *Pediatrics* 2004;114:e68–e73. URL: <http://www.pediatrics.org/cgi/content/full/114/1/e68>; *hepatitis A virus, hepatitis, infectious diseases, Mexican Americans, Hispanic Americans, migrants, pediatrics.*

ABBREVIATIONS. HAV, hepatitis A virus; CDC, Centers for Disease Control and Prevention; anti-HAV, antibody to hepatitis A

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virus; Ig, immunoglobulin; OR, odds ratio; CI, confidence interval; aOR, adjusted odds ratio; ACIP, Advisory Committee on Immunization Practices.

Despite declining rates in the United States, hepatitis A is one of the most frequently reported vaccine-preventable diseases, surpassing rubella, pertussis, and measles. In 1997, >30 000 people, including 11 000 children younger than 18 years, were reported with acute hepatitis A.¹ After these data were adjusted for anicteric infection and underreporting, an estimated 246 000 children were infected with hepatitis A virus (HAV) in 1997² (unpublished data, Centers for Disease Control and Prevention [CDC]). Hispanic children have among the highest rates of hepatitis A. In 1997, the rate among Hispanic children was 46.7 cases per 100 000, >10 times the rate among non-Hispanic white and black children.¹

In the United States, the Hispanic population is now the largest minority group, representing 13.3% of the population.³ The 2000-mile United States–Mexico border is one of the world's busiest international boundaries, with an estimated 320 million legal northbound border crossings annually.⁴ The US and Mexico border areas have a combined population of >11 million people, many of whom cross the border frequently in both directions to visit family and friends, shop, work, attend school, or seek medical care.⁵ From 1990 to 1997, the incidence rate of hepatitis A in US border counties was >3 times higher than in nonborder US states.⁶

In 1997, Hispanics represented 25% of the San Diego County population; however, they accounted for 37% of the reported cases of hepatitis A. From 1990 through 1997, an average of 105 cases of hepatitis A occurred annually among Hispanic children younger than 18 years in San Diego County. The rate of hepatitis A among Hispanic children ranged from 37 to 62 cases per 100 000 (average annual rate: 48 cases per 100 000), >3 times the national average for children (14 cases per 100 000) and 4 times the rate of Hispanic adults and non-Hispanic white and black children who live in San Diego (unpublished data, CDC).

In seroprevalence surveys conducted in rural border areas and colonias, unincorporated border communities, hepatitis A has been associated with limited sanitary infrastructure and crowded living

conditions.⁷⁻⁹ In contrast, San Diego County is primarily an urban border area with basic sanitary infrastructure available to most residents; risk factors for hepatitis A in communities such as San Diego have not been studied. We conducted a case-control study among Hispanic children in San Diego County to examine possible sources of exposure for acute hepatitis A, including child care, food and waterborne exposures, cross-border and other international travel, and travel-related activities.

METHODS

Cases were defined as Hispanic children who were younger than 18 years and were reported to the San Diego County Health Department with acute hepatitis A from June 1998 through August 2000. Hepatitis A was defined as an acute illness with 1) discrete onset of symptoms and 2) jaundice or elevated serum aminotransferase levels and a positive test for immunoglobulin (Ig) M antibody to hepatitis A virus (anti-HAV).¹⁰ Hispanic ethnicity was determined by the parent or guardian. Risk factor information was collected for the 2- to 6-week exposure period before the onset of symptoms of hepatitis A.

A case-control study was conducted with 1 to 3 control subjects per case patient. Control participants were Hispanic children who were younger than 18 years and tested negative for anti-HAV IgG in saliva. Potential control subjects were identified primarily through community health presentations at local public schools and through recruiting volunteers by visiting neighborhoods in the areas of San Diego County where most case-patients resided. A small number of control participants were identified through case-patient families, who referred nonhousehold friends and acquaintances to the County Health Department for possible participation in the study. One child per control family was selected for participation. When the family had >1 child in a particular age category, the child with the most recent birthday was chosen, except for 18 pairs of children for which 1 was randomly selected for analysis. For determining the immune status of potential control subjects, saliva specimens were collected by trained study personnel and were tested for anti-HAV IgG at the London Public Health Laboratory Service Virus Reference Laboratory according to procedures described.^{11,12} Children who tested positive for anti-HAV IgG were excluded. Potential control subjects were also excluded when they had a history of hepatitis A vaccination, a previous or recent illness with jaundice, or contact with a known case of hepatitis A during the exposure period or the preceding 2 months. Control subjects were frequency-matched to cases by age group (≤ 2 years, 3-5 years, 6-12 years, and 13-17 years), and exposure data were collected for the same 2- to 6-week period as for frequency-matched cases. All susceptible control subjects were offered hepatitis A vaccine at no cost.

Trained, bilingual community outreach workers from the health department administered the questionnaire. The questionnaires and consent forms were administered in Spanish, English, or both, based on the participants' preference. For children ≥ 14 years of age, the questionnaire was administered to the child and a parent or legal guardian. For children <14 years of age, the questionnaire was administered to a parent or legal guardian. Case-patients were interviewed either by telephone or during a visit to the home; control participants were interviewed during a visit to the home. Community outreach workers collected information about demographic characteristics and potential sources of exposure, including child care attendance, international travel and border crossing, and possible food-borne sources of infection.

The study protocol was reviewed and approved by the Committees on Protection of Human Subjects of San Diego State University and the CDC. Informed consent was obtained from a parent or legal guardian, and assent from the child was obtained for each child ≥ 7 years of age.

Data were entered in Epi Info (version 6.0; CDC) and analyzed in SAS (version 8.02; SAS Institute Inc, Cary, NC). For the case-control study, demographic and risk factor data were examined by using Pearson χ^2 , and odds ratios (ORs) and exact 95% confidence intervals (CIs) were calculated. Variables significant at $\alpha \leq .10$ were used to develop a logistic regression model using stepwise selection. Variables were included in the final model when $P < .05$

or when the variable contributed to the fit of the model based on the likelihood-ratio test.

RESULTS

From June 1998 through August 2000, 170 cases of hepatitis A among Hispanic children were reported to the San Diego County Health Department. Of these, 143 (84.1%) people could be located and were enrolled and 132 cases were analyzed; 11 people who were secondary household contacts to index cases were excluded from the analysis.

Of 444 potential control subjects identified, 354 (79.7%) were susceptible on the basis of saliva antibody testing and were enrolled; 77 (17.3%) were immune, and 13 (2.9%) were indeterminate. There were no significant differences in demographic characteristics or potential sources of exposure among the control subjects who were recruited by different methods (data not shown).

Among the cases, 3% were <2 years of age, 22% were 3 to 5 years of age, 57% were 6 to 12 years of age, and 18% were 13 to 17 years of age. The cases and control subjects had similar gender distribution and access to health insurance; approximately half of the participants were male, and one third were uninsured (Table 1). Twenty-one percent of the cases reported contact with a person with known or suspected hepatitis A infection. The case families had higher parental education and family income levels. Sixty-nine percent of the cases had an annual family income >\$15 000, compared with 21% of the control subjects (OR: 8.7; 95% CI: 5.5-13.6). Sixty percent of the cases had parental education level >12th grade compared with 13% of the control subjects (OR: 10.1; 95% CI: 6.3-16.1). The mothers of case children were more likely than mothers of control children to have been born in the United States (14% vs 3%; OR: 4.5; 95% CI: 2.1-9.6).

Sixty-seven percent of the children with hepatitis A traveled outside the United States during the incubation period, compared with 25% of the control participants (OR: 6.3; 95% CI: 4.0-9.7). All of the children had traveled to Mexico, except for 1 child with hepatitis A who had traveled to Guatemala and 1 child who had traveled to both Mexico and Guatemala. Among the children who traveled, 82% of the cases and 80% of the control subjects had traveled to Tijuana, Mexico. Travel occurred frequently during summer and Christmas holidays; consistent with the incubation period of hepatitis A virus, the number of cases increased 1 to 2 months after peaks in travel (Fig 1).

In univariate analysis among the subgroup of study participants who reported traveling during the incubation period, 85% of the children with hepatitis A ate food from a street vendor or taco stand, compared with 40% of the control participants (OR: 8.9; 95% CI: 4.3-18.3). Hepatitis A was associated with the consumption of several food items, including lettuce, salsa, water, and ice, during the trip. Cases were twice as likely to report shopping as the primary reason for their trip and were less likely to report visiting friends or family. The duration of the trip did not differ significantly among case and con-

TABLE 1. Demographic Characteristics and Potential Sources of Hepatitis A, Case-Control Study, San Diego, California, June 1998 to August 2000

Factor	Cases (n = 132)		Controls (n = 354)		Univariate OR	95% CI
	n	%	n	%		
Age group, y						
≤2	4	3.0	22	6.2		
3–5	29	22.0	99	28.0		
6–12	75	56.8	198	55.9		
13–17	24	18.2	35	9.9		
Male gender	71	54	169	45	1.4	0.9–2.1
Born in United States						
Child	120	91	297	84	1.9	1.0–3.7
Mother	18	14	12	3	4.5	2.1–9.6
Father	13	11	36	10	1.1	0.6–2.2
Family income >\$15 000	90	69	72	21	8.7	5.5–13.6
Parental education >12 y	78	60	45	13	10.1	6.3–16.1
Uninsured	48	37	150	43	0.8	0.5–1.2
Child traveled internationally	89	67	88	25	6.3	4.0–9.7
Household visitor from outside United States	12	9	58	16	0.5	0.3–1.0
Child attended child care	12	9	41	12	0.8	0.4–1.5
Household member employed in child care setting	2	2	44	12	0.1	0.1–0.5
Activities during international trip	(n = 89)		(n = 88)			
Duration of travel ≥4 d	39	44	26	30	1.9	1.0–3.5
Eating at street vendor/taco stand	76	85	35	40	8.9	4.3–18.3
Traveled for shopping	52	58	36	41	2.0	1.1–3.7
Traveled to visit family/friends	48	54	65	74	0.4	0.2–0.8
Foods consumed on trip						
Lettuce	79	89	39	44	9.9	4.6–21.7
Salsa	74	83	30	34	9.5	4.7–19.4
Water	87	98	76	86	6.9	1.5–31.7
Ice	66	74	41	47	3.3	1.8–6.2
Ceviche/raw shellfish	13	15	49	56	0.1	0.1–0.3
Fruit juice	25	28	69	78	0.1	0.1–0.2

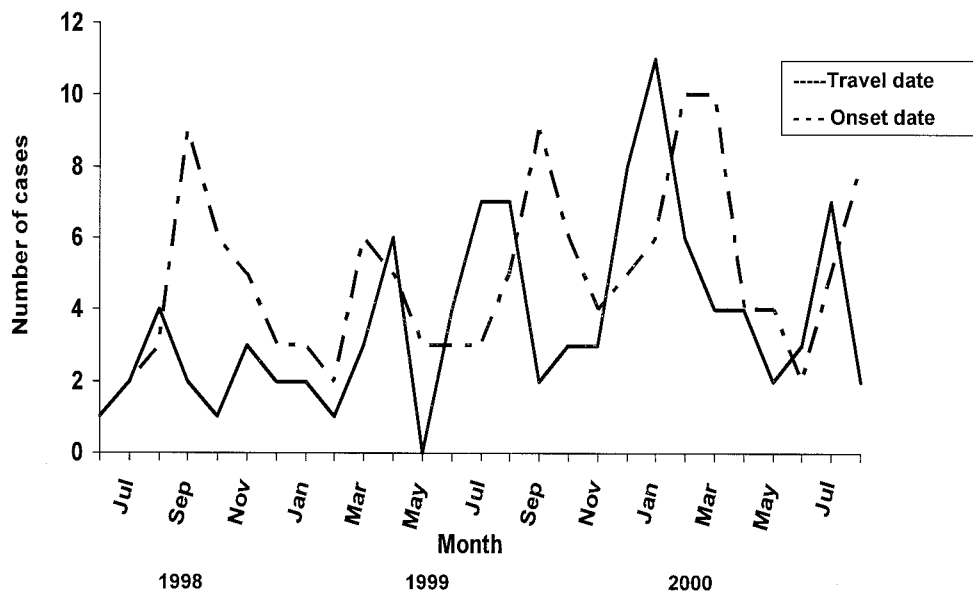


Fig 1. Hepatitis A symptom onset by date of international trip, San Diego, California, June 1998 to August 2000. A total of 132 children made 100 trips (11 children made >1 trip).

control children. Case and control participants did not differ with regard to the country of birth of the child or the father, child care attendance, household contact with someone who works in child care, or household exposure to a visitor from Mexico or another endemic country.

In multivariate analysis, children whose family had an annual income >\$15 000 (adjusted OR [aOR]:

5.3; 95% CI: 2.6–10.9) and parental education >12 years of schooling were >5 times as likely to develop acute hepatitis A (aOR: 5.2; 95% CI: 2.5–10.7; Table 2). Children with hepatitis A were less likely to have a visitor from outside the United States. Although travel outside the United States was not independently associated with hepatitis A, activities during travel were associated with infection. Children with

TABLE 2. Independent Risk Factors for Hepatitis A, San Diego, California, June 1998 to August 2000

Risk Factor	aOR	95% CI	P Value
Family income >\$15 000	5.3	2.6–10.9	<.0001
Parental education >12 y	5.2	2.5–10.7	<.0001
Household visitor from outside United States	0.3	0.1–0.9	.04
Eating at street vendor/taco stand during international travel	17.0	4.1–71.1	.0001
Eating salad/lettuce during international travel	5.2	1.3–20.1	.02
Eating ceviche/raw shellfish during international travel	0.3	0.1–0.9	.04
Drinking juice during international travel	0.1	0.1–0.3	.0001

acute hepatitis A were 17 times as likely to have eaten food from a street vendor or taco stand during travel (aOR: 17.0; 95% CI: 4.1–71.1) and >5 times as likely to have eaten salad/lettuce during travel (aOR: 5.2; 95% CI: 1.3–20.1) than control subjects. Children with hepatitis A were less likely to have consumed ceviche/raw shellfish or fruit juice than control subjects. Consumption of water or ice and reason for the trip were not independent risk factors for hepatitis A.

DISCUSSION

Historically, HAV in the United States has been spread primarily by person-to-person transmission during cyclical, community-wide outbreaks. Among cases reported to the CDC, the most frequently identified source of infection is household or sexual contact with a person with hepatitis A. International travel accounts for <10% of cases.¹³ However, in this study of Hispanic children who live along the United States–Mexico border, two thirds of children with hepatitis A reported traveling during the incubation period, principally to Mexico, and only a minority reported having had contact with a person with hepatitis A. Travel-related exposures, especially eating food from street vendors, were the factors most strongly associated with hepatitis A.

The results of this study are consistent with surveillance data collected in the Sentinel Counties Study, a population-based study of acute hepatitis in 6 nonborder US counties. From 1998 through 2000, 47% of Hispanic children younger than 18 years reported international travel to a country of intermediate or high hepatitis A endemicity, compared with <3% of non-Hispanic children and 17% of Hispanic adults. Of Hispanic children who traveled internationally, 85% traveled to Mexico and the remainder traveled to Central or South America or the Caribbean (unpublished data, CDC).

Our findings validate assumptions about the risk of acquiring hepatitis A from foods obtained from certain sources, such as street vendors, and from eating uncooked vegetables and fruits during travel to an endemic country. Hepatitis A has been associated with consumption of produce imported from Mexico, including strawberries¹⁴ and green onions.^{15,16} Food consumption during international travel and consumption of foods imported from Mexico have been associated with other enterically transmitted pathogens, including *Escherichia coli*, *Shigella sonnei*, and other organisms that cause travelers' diarrhea.^{17,18} In this study, eating lettuce was associated with hepatitis A, and the association with eating

at a taco stand may in part be attributed to exposure to lettuce, used as a garnish for tacos, a popular food item in this population.

Hepatitis A was not associated with household exposure to a visitor from Mexico or another endemic country, child care attendance, or household contact with someone who works in child care. In contrast to other studies that have shown an association between HAV infection and lower socioeconomic status,^{7,19,20} our study demonstrated an increased risk for children of higher socioeconomic status. One possible explanation is that families with higher socioeconomic status have greater resources to travel across the border and shop, the primary reason for travel for the majority of the cases.

The findings of this study represent another example of the heterogeneity of the epidemiology of hepatitis A in the United States.²¹ In a study conducted in Salt Lake City during a community-wide outbreak, transmission was associated with the presence of young children in the household.²² In Maricopa County, Arizona, child care exposure has been the major risk factor.²³ In other communities, transmission has been associated with outbreaks among men who have sex with men or illicit drug users.²¹ Even along the United States–Mexico border, the epidemiology of hepatitis A reflects diverse local conditions; for example, access to basic sanitation is likely still a factor in the colonias and rural areas along the border,^{7–9} whereas international border travel and activities during travel may be more important for the urban border residents, as demonstrated in this study. Furthermore, it is not known whether the specific travel-related activities associated with hepatitis A are similar among children who travel from border compared with nonborder areas. For example, people who travel greater distances may be more likely to stay overnight in the homes of friends and family, providing opportunities for person-to-person transmission from household contacts with hepatitis A.

The results of this study are limited by several factors. The case and control participants were interviewed several weeks to months after the 2- to 6-week exposure period, increasing the likelihood of recall bias. Although they received standardized training to minimize variability in administering the questionnaire, several different project staff interviewed case and control participants. Furthermore, control participants were interviewed during a visit to the home, whereas case participants were interviewed by telephone or during a visit to the home.

Potential control participants were identified by various methods; therefore, they may not be entirely comparable to the case participants. In addition, the results may not be generalized to other border communities or to Hispanic children who live outside the border region. Last, we could not evaluate the role of having contact with a case participant as a risk factor because these people were excluded as control participants from the study.

We used a saliva-based assay to identify and exclude immune children as controls. This assay was developed in the United Kingdom more than a decade ago and has been shown to have high sensitivity and specificity for detecting immunity from naturally acquired infection.^{11,12} Its properties are suitable for use in nonclinical settings, and it has been used in other field studies to identify immune potential control subjects.^{24,25} Inclusion of a small number of immune children with false-negative results on the salivary assay would be unlikely to affect substantially our results.

Hepatitis A vaccine was licensed in the United States in 1995. In 1996, the Advisory Committee on Immunization Practices (ACIP) published the first recommendations for hepatitis A vaccination of high-risk individual, including people who travel to endemic countries and people who live in certain racial and ethnic communities with the highest rates of hepatitis A, such as American Indian, Alaska Native, and selected Hispanic, migrant, and religious communities.²⁶ In 1999, the ACIP expanded the recommendations to routine vaccination of all children who live in states, counties, or communities where the average annual rate during the baseline period of 1987 to 1997 was ≥ 20 cases per 100 000 (twice the national average of ~ 10 cases per 100 000) and to consider routine vaccination of all children in areas with a rate of 10 to 19 cases per 100 000.²⁷

Despite the vaccination recommendation for international travelers to endemic countries such as Mexico, in place at the time this study was conducted, it is likely that few traveling children received vaccine. In 1998, only 20 doses of hepatitis A vaccine were administered in the public sector in San Diego County and no potential control subjects were excluded from this study because of a history of vaccination. Both border residents and their health care providers may not consider travel across the border as international travel. After the ACIP recommendations in 1999, San Diego County began offering hepatitis A vaccination at little or no cost in public clinics to all children of 2 to 18 years of age. By 2001, the number of doses of hepatitis A vaccine administered in the public clinics increased to 72 410 doses, which could cover $\sim 6\%$ to 11% of the pediatric population in San Diego (unpublished data, San Diego County Health and Human Services Agency). However, data about actual vaccine coverage or the use of vaccine in the private sector are not available.

Similar to national trends, the overall incidence rate of hepatitis A in San Diego County has declined since 1999 and reached 6.2 cases per 100 000 in 2002. Among Hispanic children in San Diego County, rates have remained high through 2000 but since have

declined $\sim 70\%$, from 39.9/100 000 in 2000 to 12.1/100 000 in 2002. This decline may reflect, at least in part, implementation of the recommendations for routine vaccination of children (unpublished data, CDC).

The role of international travel in the transmission of various diseases among immigrants and their children, who are returning to their country of origin to visit friends and relatives, has been demonstrated for other diseases, including malaria.^{28,29} These populations have been difficult to target for pretravel medical care and vaccination for other diseases.^{30,31} Primary care pediatricians and other clinicians who care for Hispanic children who reside in areas where routine vaccination is not currently recommended should be aware of the need to inquire about international travel among Hispanic children. Clinicians should give hepatitis A vaccine to pediatric travelers to endemic countries and provide other preventive counseling, including guidance about safe water and food consumption and the avoidance of food from street vendors. Additional studies should be conducted among Hispanic children who reside in non-border communities to better understand the epidemiology of hepatitis A, including the role of international travel and travel-related activities.

Despite evidence of hepatitis A vaccination of some children in response to the recommendation for routine vaccination, coverage remains low in San Diego and the majority of eligible children remain unvaccinated. Except for the Texas border region and limited areas in Arizona, hepatitis A vaccination of children in US border states is recommended but not mandated; thus, it is likely that coverage is low. This study highlights the importance of full implementation of routine vaccination of children in areas in which it is recommended.

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