ABSTRACT. Objective. To evaluate the role of child care centers in a community-wide outbreak of hepatitis A epidemic.

Methods. We analyzed surveillance data during an epidemic in Maricopa County, Arizona, from January to October 1997 and conducted a case-control study using a sample of cases reported from June to November. Cases were physician-diagnosed and laboratory confirmed; for this analysis we used the Arizona Office of Child Day Care Licensing. Surveillance data were linked to the child care center list to determine which centers had reported hepatitis A cases. We conducted univariate and multivariate conditional logistic analyses and calculated population attributable risks (PAR).

Results. In total, 1242 cases (50/100 000 population) were reported. The highest rates occurred among people aged 0 to 4 (76/100 000), 5 to 14 (95/100 000), and 15 to 29 (79/100 000) years. The most frequently reported risk factor was contact with a hepatitis A patient (45%). However, nearly 80% of these contacts were with individuals who attended or worked in a child care center. Overall, child care center–related contact could have been the source of infection for 34% of case-patients. In the case-control study, case-patients (n = 116) and control subjects (n = 116) did not differ with respect to demographic characteristics. A total of 51% of case-patients compared with 18% of control subjects reported attending or working in a child care setting (direct contact; adjusted odds ratio [OR]: 6.0; 95% confidence interval [CI]: 2.1–23.0) or being a household contact of such a person (indirect contact; OR: 3.0; 95% CI: 1.3–8.0). In age-stratified analyses, the association between hepatitis A and direct or indirect contact with child care settings was strongest for children <6 years old and adults aged 18 to 34 years. Household contact with a person with hepatitis A also was associated with hepatitis A (OR: 9.2; 95% CI: 2.6–58.2). The presence of a child <5 years old in the household was not associated with hepatitis A. The estimated PAR for direct child care contact was 23% (95% CI: 16–34), for indirect child care contact was 21% (95% CI: 13–35), and for any child care contact was 40% (95% CI: 30–53). Information on 1243 licensed child care centers was obtained, with capacity ranging from 5 to 479 slots (mean: 87). Thirty-four (2.7%) centers reported hepatitis A cases. Centers that had a mean capacity of >50 children were more than twice as likely to have had a reported case of hepatitis A (OR: 2.6; 95% CI: 1.1–6.7). Among the 747 centers that accepted >50 children, having infant (OR: 3.7; 95% CI: 1.6–8.3), toddler (OR: 6.3; 95% CI: 2.2–20.0), or full-day service (OR: undefined; 95% CI: 1.7–40) was associated with having a reported case of hepatitis A.

Conclusions. In Maricopa County, people associated with child care settings are at increased risk of hepatitis A, and child care attendees may be an appropriate target group for hepatitis A vaccination. Considering the estimated proportion of children who attended child care and were old enough to receive hepatitis A vaccine (≥2 years of age) and the calculated PAR, approximately 40% of cases might have been prevented if child care center attendees and staff had been vaccinated. However, epidemiologic studies indicate that the proportion of cases that are attributable to child care center exposure varies considerably among counties, suggesting that this exposure may be associated with an increased risk of hepatitis A in some communities but not in others. To prevent and control hepatitis A epidemics in communities, the Advisory Committee on Immunization Practices and the American Academy of Pediatrics have adopted a long-term strategy of routine vaccination of children who live in areas with consistently elevated hepatitis A rates. After demonstrating cost-effectiveness, a rule was implemented in January 1999 to require hepatitis A vaccination of all children who are aged 2 to 5 years and enrolled in a licensed child care facility in Maricopa County. Other communities with similar epidemiologic features might consider routine vaccination of child care center attendees as a long-term hepatitis A prevention strategy. Consistent with current recommendations, in communities with persistently elevated hepatitis A rates where child care center attendance does not play an important role in hepatitis A virus transmission in the community, child care centers may nonetheless provide a convenient access point for delivering hepatitis A as well as other routine childhood vaccinations. Pediatrics 2001;108(5). URL: http://www.pediatrics.org/cgi/content/full/108/5/e78; hepatitis A, immunization, child care.

ABBREVIATIONS. IG, immune globulin; HAV, hepatitis A virus; OR, odds ratio; CI, confidence interval; PAR, population attributable risk.

Hepatitis A is a common, vaccine-preventable disease in the United States, with an estimated 80 000 to 90 000 cases occurring each year. Most hepatitis A occurs in the context of community-wide epidemics during which infection is
transmitted from person to person by the fecal-oral route. The highest rates of disease are seen among children and young adults, and asymptomatic infection among young children is common.

These community-wide epidemics have been difficult to control. Although immune globulin (IG) is recommended to protect exposed individuals and control outbreaks in child care centers, it has had limited effectiveness in controlling community-wide epidemics. Hepatitis A vaccine, licensed in the United States since 1995 for use in people aged 2 years and older, provides a new tool for preventing and controlling community-wide epidemics.

In 1997, a hepatitis A epidemic began in Maricopa County, Arizona. We conducted an investigation to determine the source of the epidemic and the role that child care attendance played in sustaining the epidemic among children and adults.

BACKGROUND

Maricopa County (greater Phoenix), Arizona, has experienced periodic community-wide epidemics of hepatitis A approximately every 10 years, with peak incidence rates reaching approximately 70 per 100 000 population (Centers for Disease Control and Prevention, unpublished data). Surveillance data collected during one such epidemic during 1977 to 1980 indicated that 30% of hepatitis A cases resulted directly from child care center–associated outbreaks and that child care–associated hepatitis A may have played a role in sustaining the outbreak in the rest of the community.

During the first 6 months of 1997, Maricopa County experienced a >50% increase in the number of reported hepatitis A cases compared with the same time period in the previous year. Outbreaks were reported in a number of child care centers. Attempts to use IG to control hepatitis A in these centers were mostly unsuccessful; only 20% of people for whom administration of IG was recommended received it. This was attributable mostly to a lack of aggressive outreach and a shortage of IG at the time. As the number of reported cases continued to rise, we undertook an investigation that sought to describe the epidemiology of the ongoing community-wide epidemic, evaluate the role of child care center–associated hepatitis A in sustaining the epidemic, and identify groups that are at risk for hepatitis A and that could be targeted for a vaccination program.

METHODS

Descriptive Epidemiology

A case was defined as a resident of Maricopa County who was reported to have IgM antibody to hepatitis A virus (anti-HAV) between January 1 and October 31, 1997. Cases were reported to the Maricopa County Health Department and the Arizona Department of Health Services by laboratories and health care providers. Data collected on all cases included date of onset, age, gender, race/ethnicity, and home address. Information regarding potential risk factors, such as contact with child care centers, international travel, and injecting drug use, was collected for reported cases with onset of symptoms between July 1 and October 31. Incidence rates were calculated using 1990 population denominators provided by the US Census Bureau.

Case-Control Study

A case-control study was conducted by telephone to evaluate possible associations between contact with child care centers and hepatitis A. A case was defined as a resident of metropolitan Phoenix, with onset of provider-diagnosed hepatitis A between June 1 and November 30, 1997, who was IgM anti-HAV positive. When >1 case was reported in a household, 1 was randomly chosen. Case-patients without a telephone or with an incorrect telephone number or who could not be reached by telephone after 3 attempts were excluded. One control subject was frequency matched to each case by age group and neighborhood using a reverse telephone directory. Control subjects were excluded if they had a history of hepatitis A or had received IG in the previous 6 months or hepatitis A vaccine. Case-patients and their matched control subjects (or parent/guardian if <18 years old) were asked demographic information and about potential risk factors in the 2 to 6 weeks before illness onset date or, in the case of control subjects, the onset date of the matched case. Potential risk factors included close personal contact with a person with hepatitis A, work or attendance at a child care center (direct child care contact), work or attendance of a household member in a child care setting (indirect child care contact), other contact with diapered children, travel outside the United States, use of street drugs, and sexual preference. Sample size calculations indicated that a total of 116 matched pairs were necessary to detect an odds ratio (OR) of ≥2.0 with α = 0.05 and a power of 80%.

Child Care Center Characteristics

Characteristics of all licensed child care centers in Maricopa County were obtained through review of computerized lists from the Arizona Office of Child Day Care Licensing. Information was available on the maximum number of children legally allowed in the facility (capacity), hours of service, whether the center provided infant (<1 year of age) and/or toddler (1–3 years of age) services, type of facility (licensed home child care, child care center, Head Start, etc), and location. Surveillance data were linked to the child care list to determine which centers had reported cases of hepatitis A.

Analysis and Statistics

To examine potential associations between individual variables and hepatitis A, Mantel-Haenszel matched ORs were calculated. Confidence intervals (CI) were calculated according to the method of Robins et al. To identify independent risk factors for hepatitis A and control for confounding variables, we developed a conditional logistic regression model using the stepwise, forward selection method. For each factor, the population attributable risk (PAR) was estimated using the exposure rate among cases and the adjusted OR in the final model to estimate the relative risk. CIs for each PAR were calculated using a Taylor series linear approximation to estimate the standard errors.

RESULTS

Descriptive Epidemiology

The 1242 cases reported from January to October 1997 represented an overall incidence rate of 50 per 100 000 population. A total of 165 patients (13%) were hospitalized, and 1 died. The highest rates occurred in those 0 to 29 years of age (Table 1). Females accounted for 52% of cases. Among cases in which race was known, 91% were among whites, but American Indians had the highest rate. A total of 64% of cases were among non-Hispanics; however, the incidence rate was lower among non-Hispanics compared with Hispanics (Table 1).

Among the 258 patients from whom information was collected, the most frequently reported potential source of infection was household contact with a person with hepatitis A in the 2 to 6 weeks before illness onset, reported by 111 case-patients (43%). However, nearly 80% of these contacts were with
null
centers were important in sustaining HAV transmission in the community. IG was administered to all center children and employees whenever hepatitis A occurred in an employee or a child or in a parent of an attendee. The 21-month intervention resulted in a 77% overall decrease in newly reported cases of hepatitis A in the county. This study extends these observations through the use of a control group and an estimation of the PAR associated with child care contact.

Epidemiologic studies indicate that the proportion of cases that are attributable to child care center exposure varies considerably among counties, suggesting that this exposure may be associated with an increased risk of hepatitis A in some communities but not in others. Although 11% to 16% of reported cases of hepatitis A have been associated with child care center contact, and whether contact with child care centers is associated with an increased risk of hepatitis A has not been evaluated in studies using an appropriate comparison group.

Serologic surveys of child care workers have not found an increased prevalence of anti-HAV compared with an appropriate comparison group. Our investigation supports previous findings indicating that the presence of young children in diapers is a factor that may facilitate the spread of HAV in child care centers. Behavioral and environmental factors associated with diaper-wearing children may facilitate the transmission of infectious diseases. Children in this age group often mouth objects, and stool may be spread easily from diapers to the immediate environment. Other characteristics associated with hepatitis A in our investigation, including a child care capacity of 50 slots and offering full day service, are consistent with findings in previous studies. Large facilities, in which toilet-trained and non-toilet-trained children share rooms or caregivers have been shown in previous studies to be associated with more frequent transmission of infectious agents.

This investigation had several limitations. Collection of information by telephone, which excluded individuals who did not have a working telephone, may have reduced the representativeness of the study sample. However, participants and nonparticipants (those without a working telephone) did not differ with respect to their demographic characteristics. In addition, study participants may not have given accurate responses to sensitive questions about factors associated with hepatitis A, such as drug use or sexual preference. However, this would be expected to have occurred with equal frequency among case-patients and control subjects. Control subjects were not serologically tested, and some of them may have been immune to hepatitis A. However, inclusion of immune control subjects would have decreased the magnitude of the association between child care exposure and hepatitis A.

IG, coupled with the optimization of hygiene and provision of adequate facilities for diaper-changing and disposal, has been recommended for many years to control HAV transmission in child care centers and has been shown to be effective when implemented aggressively and consistently. However, a number of problems may arise when using IG to control outbreaks in child care centers. As occurred in Maricopa County, it is often difficult to administer IG in a timely manner, and acceptance is sometimes

**TABLE 2.** Selected Characteristics of Case-Patients and Control Subjects, Maricopa County, Arizona, 1997

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Case-Patients (n = 116)</th>
<th>Control Subjects (n = 116)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (y)</td>
<td>23.1</td>
<td>23.4</td>
<td>.89</td>
</tr>
<tr>
<td>Gender (female; n [%])</td>
<td>77 (67)</td>
<td>73 (63)</td>
<td>.76</td>
</tr>
<tr>
<td>Race (n [%])</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>108 (93)</td>
<td>102 (88)</td>
<td>.55*</td>
</tr>
<tr>
<td>Black</td>
<td>2 (2)</td>
<td>8 (7)</td>
<td></td>
</tr>
<tr>
<td>Other†</td>
<td>6 (5)</td>
<td>6 (5)</td>
<td></td>
</tr>
<tr>
<td>Hispanic ethnicity (n [%])</td>
<td>23 (20)</td>
<td>30 (26)</td>
<td>.31</td>
</tr>
<tr>
<td>Education &gt;12 y (n [%])</td>
<td>97 (84)</td>
<td>90 (78)</td>
<td>.18</td>
</tr>
</tbody>
</table>

* White race compared with all others.
† American Indian or Asian.

**TABLE 3.** Comparison of Hepatitis A Case-Patients and Control Subjects According to Selected Characteristics, Maricopa County, Arizona, 1997

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Case-Patients (n = 116)</th>
<th>Control Subjects (n = 116)</th>
<th>Univariate Matched OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Household contact with a person with hepatitis A</td>
<td>26 (22)</td>
<td>2 (2)</td>
<td>14 (3.4–117.0)</td>
</tr>
<tr>
<td>Direct child care contact</td>
<td>32 (28)</td>
<td>10 (9)</td>
<td>6.5 (2.3–25.0)</td>
</tr>
<tr>
<td>Indirect child care contact</td>
<td>36 (31)</td>
<td>12 (10)</td>
<td>3.7 (1.7–8.7)</td>
</tr>
<tr>
<td>Direct or indirect child care contact</td>
<td>59 (51)</td>
<td>21 (18)</td>
<td>5.8 (2.7–14.0)</td>
</tr>
<tr>
<td>Household size &gt;4 people</td>
<td>71 (61)</td>
<td>29 (25)</td>
<td>5.3 (1.8–21.0)</td>
</tr>
<tr>
<td>White</td>
<td>85 (73)</td>
<td>74 (64)</td>
<td>1.5 (0.7–3.2)</td>
</tr>
<tr>
<td>Having a child &lt;5 in the household</td>
<td>49 (42)</td>
<td>40 (34)</td>
<td>1.5 (0.8–3.0)</td>
</tr>
<tr>
<td>&gt;High school education</td>
<td>66 (57)</td>
<td>57 (49)</td>
<td>1.5 (0.8–2.9)</td>
</tr>
</tbody>
</table>
low. In addition, IG has been in short supply at times in recent years. Furthermore, the protective effect of IG is temporary, and centers with recurrent outbreaks need to be visited multiple times for IG administration.

The availability of hepatitis A vaccine provides a new tool to control and prevent hepatitis A. However, little is known about the effectiveness of hepatitis A vaccine when used without IG in controlling outbreaks in child care centers. When given after exposure, the effectiveness of hepatitis A vaccine compared with IG in preventing hepatitis A is unknown, and it is possible that vaccine would be less effective than IG in this circumstance, especially when the time since first exposure is relatively long. In addition, hepatitis A vaccines are not licensed for children <2 years old, yet young children may transmit HAV in child care centers. Although the proportion of child care attendees who are <2 years old was low in Maricopa County, it is difficult to predict to what extent the current lack of availability of a vaccine for use in children in this age group might influence the effectiveness of vaccination in controlling hepatitis A outbreaks in child care centers. Because of these unresolved issues, IG, coupled with hepatitis A vaccine when indicated, continues to be recommended for control of outbreaks in child care centers.11,12

To prevent and control hepatitis A epidemics in communities, the Advisory Committee on Immunization Practices and the American Academy of Pediatrics have adopted a long-term strategy of routine vaccination of children who live in areas with consistently elevated hepatitis A rates.11,12 The Advisory Committee on Immunization Practices indicated that routine vaccination of children in these areas could be accomplished through a variety of means, including vaccination of 1 or more single age cohorts or of children who attend child care centers.

The epidemiologic features of hepatitis A and the results of our investigation and of previous studies support the strategy of vaccination of child care attendees and workers in Maricopa County for the long-term control of hepatitis A in the community. The PAR associated with child care center attendance suggests that ongoing routine vaccination of children who attend child care centers would result in an appreciable decline in overall hepatitis A incidence over time. After demonstrating the cost-effectiveness of such a measure, a rule was implemented in January 1999 to require hepatitis A vaccination of all children who are aged 2 to 5 years and enrolled in a licensed child care facility in Maricopa County.13 Other communities with similar epidemiologic features might consider routine vaccination of child care center attendees as a long-term hepatitis A prevention strategy. Consistent with current recommendations, communities with persistently elevated hepatitis A rates where child care center attendance does not play an important role in HAV transmission in the community, child care centers may nonetheless provide a convenient access point for delivering hepatitis A as well as other routine childhood vaccinations.

REFERENCES

TABLE 4. Characteristics of Child Care Centers in Maricopa County, 1997 (n = 1243)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Child Care Centers With Cases (n = 34)</th>
<th>Child Care Centers Without Cases (n = 1209)</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean capacity &gt;50 children</td>
<td>79%</td>
<td>60%</td>
<td>2.6</td>
<td>1.1–6.7</td>
</tr>
<tr>
<td>Infant service</td>
<td>37%</td>
<td>25%</td>
<td>3.7</td>
<td>1.6–8.3</td>
</tr>
<tr>
<td>Toddler service</td>
<td>81%</td>
<td>41%</td>
<td>6.3</td>
<td>2.2–20.0</td>
</tr>
<tr>
<td>Full-day service</td>
<td>100%</td>
<td>76%</td>
<td>Undefined</td>
<td>1.7–x</td>
</tr>
</tbody>
</table>

* Centers with >50 children (n = 747).
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