An Outbreak of Hepatitis A among Health Care Workers: Risk Factors for Transmission

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Introduction

Nosocomial outbreaks of hepatitis A are relatively uncommon. Several food-related epidemics have been reported.1,2 Most nosocomial outbreaks have involved exposure either to an asymptomatic infant or to a young child, typically after the transfusion of blood from an asymptomatic donor.3-8 Occasionally, outbreak clusters have been reported after contact with an older child or adult with vomiting, diarrhea, or fecal incontinence.9-14 Several large outbreaks in neonatal intensive-care units have been reported recently.4,5,7,8 Despite extensive investigations, most previous reports failed to identify significant risk factors for nosocomial transmission, other than associated care of the infected individual. Rosenblum and colleagues9 recently reported an outbreak of hepatitis A in a neonatal intensive-care unit, implicating the behaviors of drinking beverages in the unit and failure to wear gloves routinely as risk factors for transmission to health care workers.

We report here the first nosocomial outbreak of hepatitis A in a burn treatment center. The outbreak occurred between January and March 1990 in a tertiary-care hospital. A 32-year-old man and his 8-month-old son who developed hepatitis A while in the hospital. The cumulative incidence risk ratio was elevated for health care workers caring for either the infant or the father during the same week of exposure. The case–control study implicated the behavior of eating on the hospital ward as the single most important risk factor for infection.


Background

The hospital is a 900-bed referral center with a 16-bed burn treatment center. The typical nursing staff to patient ratio on the burn treatment center is approximately 1:3, although it varies depending on the acuity of the patient and the time of day. Health care workers regularly assigned to the burn treatment center often eat in the staff lounge or in a charting room, located approximately 15–50 feet from most of the patient rooms (Figure 1). Staff food is stored in a refrigerator in a designated staff food room, the staff lounge, or occasionally in the patient nourishment room. Infants and young children with burns are allowed to play in a playpen and eat beside the desks in the center of the burn treatment area. Additionally, outpatients with burns are routinely seen in follow-up on the ward and often bring in snack foods to share with the burn treatment personnel. Two sinks are located at the entrance to the center, and hand-washing is strongly encouraged.

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on entering and leaving the ward with a display of prominent signs.

**Methods**

**Epidemic Investigation**

Selected burn treatment personnel and the burn patient with the secondary case of hepatitis were interviewed to determine potential common exposures and risk factors. The burn treatment center's charting room, staff lounge, refrigerators, sinks, ice machine, nourishment room, hydrotherapy room, rest rooms, water supply, and all patient care areas were inspected by members of the hospital epidemiology staff.

**Screening.** All health care workers assigned to the center in the prior 6 weeks (n = 154), all inpatients at the time of identification of the outbreak on February 9, 1990 (n = 12), and all patients discharged in the previous month (n = 45) were contacted and offered the option of screening with liver function tests and a serologic test for hepatitis A virus immunoglobulin M antibody (IgM anti-HAV test) (enzyme immunoassay, Abbott Laboratories, Chicago, Ill). Additionally, all food preparation workers in the hospital and the dietary services staff working on the burn center (n = 119) were contacted and similarly screened. All exposed employees of the burn treatment center who were IgM anti-HAV negative were tested for total anti-HAV antibody (anti-HAV, Abbott). A repeat IgM anti-HAV test was obtained for all consenting exposed health care workers regularly assigned to the burn treatment center 6 weeks later (n = 37) to determine whether seroconversion had occurred despite prophylaxis.

**Case definition.** A health care worker was defined as exposed if he or she had direct patient contact on the burn center in the 6 weeks (December 28, 1989, to February 7, 1990) before the outbreak. A preliminary case definition required elevation of serum levels of one of the liver transaminases to twice the upper limit of normal or symptoms consistent with acute HAV infection. Final inclusion as a case subject required a positive IgM anti-HAV titer, with or without clinical symptoms. A susceptible control subject was an exposed health care worker who tested negative for anti-HAV and who was in one of the same occupational categories as the health-care-worker case subjects (n = 60). Individuals with incomplete test results or prior immunity were excluded from further analysis.

**Immunoprophylaxis.** All asymptomatic health care workers in the burn treatment center who had contact with the index cases, all current patients, and all patients discharged in the previous month were contacted and offered immunoglobulin immunoprophylaxis. Health care workers were informed that the efficacy of immunoglobulin immunoprophylaxis has been demonstrated only when it is given within 2 weeks of exposure. Additionally, regional exchange nurses temporarily assigned to the burn treatment center to cover staffing shortages and all new patients admitted for the subsequent 6 weeks were offered immunoglobulin. All close contacts of those persons who were clinically ill or who had elevated liver transaminases were contacted to be screened and offered immunoglobulin. Consenting exposed individuals were given a single dose of immunoglobulin 0.02 ml/kg (Gamastan, Cutter Biologicals, West Haven, Conn) intramuscularly in the deltoid muscle. All case subjects were contacted by telephone 4 months later to determine whether any symptomatic secondary cases had occurred among their family members or close contacts.

Four burn treatment center nurses had been "pulled" to staff four other intensive-care units in the 48 hours before they became clinically ill. The patients for whom they cared and health care workers in close contact with the infected nurses were contacted and offered immunoglobulin prophylaxis.

**Index cases investigation.** The source of the initial index cases was investigated by interviewing the adult index case patient and his family members regarding potential risk factors and any possible common sources of exposure to hepatitis A before admission to the hospital. The Iowa State Health Department inspected a single family day-care home that cared for the index infant and six other children before the outbreak. Serum was obtained for an anti-HAV test from five of the six children, the babysitter, and family members of the babysitter. However, a sample could not be obtained from one of the children. Additionally, blood bank records were reviewed to determine the individuals donating blood to the two index case patients. None of the donors had given blood to both patients; all were contacted and asked to report any clinical illness in the 2 months before their donations.

**Patient care study.** A retrospective cohort study of health care workers was performed to evaluate the risk of infection associated with caring for the patients with the index cases. Nursing care assignments for the 6 weeks before the period of the peak incidence were examined to determine which nursing personnel had been
exposed to the index case patients. The study population included nurses and nursing students working in the burn treatment center during the 6-week period. Serosusceptible nurses caring for either of the index case patients were classified as exposed if assignment to one of the index patients occurred at least 2 weeks before the development of illness by the health care worker. Adjusted infection rates by week of exposure were calculated and were stratified by the number of shifts worked with either or both of the patients. Cumulative incidence ratios (relative risk ratios) were also calculated by week of exposure to either index patient.

Risk factor study. A case–control study was performed to evaluate behavioral risk factors and common exposures among health care workers for development of hepatitis A infection. A 50-item self-administered questionnaire was developed to assess potential risk factors for hepatitis A infection such as patient care practices (e.g., hand-washing, glove use, providing hydrotherapy, specific types of care of infants and adults), personal habits while working (e.g., eating, drinking, smoking, biting fingernails), any group exposures (e.g., potlucks, shared meals, dining out), environmental exposures, and specific food items eaten while at work. The questionnaire was pretested, revised, and then mailed to all 154 health care workers assigned to work in the burn treatment center in the 6 weeks before the outbreak’s peak. All questionnaires were identified only by a confidential study number known to the investigators. Three sequential mailings of the questionnaire, which were followed by telephone contacts, were used to improve the response rate.

Statistical Methods

The statistical analyses included the use of the Mantel-Haenszel chi-square statistic, Fisher’s two-tailed exact test, and odds ratios with 95% confidence intervals for all significance testing.16 For the tables with zero entries, 0.5 was added to each cell; the Mantel-Haenszel estimator of the odds ratio and the test-based confidence interval were determined. Stepwise logistic regression was conducted by using SAS17 to evaluate all variables that were identified by the univariate approach \((P < .10)\). The significance level was set at .05. All \(P\) values reported are two-tailed.

Results

The IgM anti-HAV test was positive in the adult index case patient 1 month after admission. His asymptomatic 8-month-old son was also IgM anti-HAV positive at the same time. Serologic tests for hepatitis A (IgM-specific and total anti-HAV antibody) and liver function tests for both patients had been negative on admission. At the time of the investigation, no additional blood samples were available for antibody testing from the first month of the patients’ hospitalization. Neither patient had vomiting or diarrhea. Inspection of the burn treatment center revealed sinks and dispensers for hand-cleansing agents located in each room, and all were found to be in good repair. Boxes of gloves and gowns and masks were readily available in each patient’s room. All burn treatment personnel were asked to refrain from eating or drinking on the ward after identification of the outbreak.

A total of 154 health care workers were identified as having been exposed to patients on the burn treatment center in the 6 weeks before the health care workers became ill. Serologic tests for anti-HAV antibody in all consenting exposed workers demonstrated that only 8.7% of the 126 workers screened had detectable immunoglobulin G antibody to the hepatitis A virus. Three health care workers with clinical hepatitis A infection and the secondary case patient were initially seronegative for IgM anti-HAV antibody despite symptoms and elevated hepatic transaminases, but subsequently became seropositive in 5 to 7 days.

Eventually a total of 11 health care workers developed IgM anti-HAV antibody, and all became clinically ill (Figure 2). Two required hospitalization for dehydration. The infection rates among serologically defined susceptible individuals ranged from 14% (7 of 50) among staff nurses and nursing assistants to 33% (2 of 6) among ward clerks and 67% (2 of 3) among nursing students. All case subjects had contact with the infant, whereas only 8 of 11 case subjects (73%) also had contact with the father. The 32-year-old mother of the index infant was also seropositive for IgM anti-HAV antibody, but remained asymptomatic. No symptomatic secondary cases occurred in close contacts or family members of the infected case subjects. The mother of the child was seropositive when checked in early February, although she was asymptomatic. One asymptomatic seroconversion occurred after prophylaxis with immunoglobulin in the fiancé of one of the nurse case subjects. None of 37 seronegative health care workers whose serology was rechecked at 4 to 6 weeks developed anti-HAV antibody.

Importantly, four cases of hepatitis A occurred in the county of residence of the infant and his father during November 1989, followed by 8 and 17 cases, respec-
Do eing of clustering county noted at 1682 American 3-Selcon FIGURE Note. Noe. Seronegative HCWs (Anti-HAV Ab) HCWs consenting to serologic screening Seronegative HCWs (Anti-HAV Ab) HCWs returning questionnaire HCWs in same occupational class as cases Note. The selection of serosusceptible control subjects whose occupations were similar to those of the case subjects. The number of control subjects remaining after each selection is shown. HCWs = health care workers.

FIGURE 3—Selection of study control subjects.

TABLE 1—Hepatitis A among Health Care Workers in a Burn Treatment Center, January-February 1990: A Case-Control Questionnaire Study on Risk Factors

<table>
<thead>
<tr>
<th>Exposure Variable</th>
<th>Case Subjects</th>
<th>Control Subjects</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eating food on the burn center (BC) (frequently vs occasionally or never)</td>
<td>10</td>
<td>1</td>
<td>24 34</td>
<td>14.2</td>
</tr>
<tr>
<td>Bringing in snacks to share in prior 6 weeks</td>
<td>7 4</td>
<td>10 50</td>
<td>8.8</td>
<td>2.44, 31.34</td>
</tr>
<tr>
<td>Eating snacks brought in by coworkers</td>
<td>10 1</td>
<td>36 24</td>
<td>6.7</td>
<td>0.99, 44.48</td>
</tr>
<tr>
<td>Close contact with mother of infant</td>
<td>2 9</td>
<td>2 58</td>
<td>6.4</td>
<td>0.99, 41.95</td>
</tr>
<tr>
<td>Providing hydrotherapy</td>
<td>9 2</td>
<td>26 34</td>
<td>5.9</td>
<td>1.33, 26.13</td>
</tr>
<tr>
<td>Spending ≥3 hours daily with BC patients</td>
<td>9 2</td>
<td>27 33</td>
<td>5.5</td>
<td>1.23, 24.62</td>
</tr>
<tr>
<td>Working in the tub room</td>
<td>9 2</td>
<td>29 31</td>
<td>4.8</td>
<td>1.06, 21.88</td>
</tr>
<tr>
<td>Care of infants: playing</td>
<td>11 0</td>
<td>52 8</td>
<td>3.7</td>
<td>0.20, 69.23</td>
</tr>
<tr>
<td>Eating food from the common refrigerator</td>
<td>9 2</td>
<td>32 28</td>
<td>3.9</td>
<td>0.85, 18.34</td>
</tr>
<tr>
<td>Drinking coffee prepared on the BC</td>
<td>8 3</td>
<td>26 34</td>
<td>3.5</td>
<td>0.88, 13.78</td>
</tr>
<tr>
<td>Care of infants: holding/carrying</td>
<td>11 0</td>
<td>53 7</td>
<td>3.2</td>
<td>0.17, 60.55</td>
</tr>
<tr>
<td>Eating at a BC potluck</td>
<td>3 8</td>
<td>9 51</td>
<td>2.1</td>
<td>0.48, 9.43</td>
</tr>
<tr>
<td>Eating out with coworkers in prior 6 weeks</td>
<td>4 7</td>
<td>14 44</td>
<td>1.8</td>
<td>0.37, 8.39</td>
</tr>
<tr>
<td>Chewing on pens or pencils</td>
<td>4 7</td>
<td>15 45</td>
<td>1.7</td>
<td>0.44, 6.68</td>
</tr>
<tr>
<td>Eating cookies made by index patients’ family</td>
<td>3 8</td>
<td>13 47</td>
<td>1.4</td>
<td>0.31, 5.89</td>
</tr>
<tr>
<td>Care of infants: physical therapy</td>
<td>8 3</td>
<td>41 19</td>
<td>1.2</td>
<td>0.29, 5.23</td>
</tr>
<tr>
<td>Smoking</td>
<td>3 8</td>
<td>13 47</td>
<td>1.4</td>
<td>0.31, 5.89</td>
</tr>
<tr>
<td>Care of infants: dressing changes</td>
<td>9 2</td>
<td>48 12</td>
<td>1.3</td>
<td>0.21, 5.97</td>
</tr>
<tr>
<td>Eating cafeteria food on the BC</td>
<td>10 1</td>
<td>56 4</td>
<td>0.7</td>
<td>0.07, 7.12</td>
</tr>
<tr>
<td>Biting fingernails</td>
<td>1 1</td>
<td>10 44</td>
<td>0.3</td>
<td>0.04, 2.42</td>
</tr>
</tbody>
</table>

Note. All of the control subjects did not respond to each questionnaire item, so the total number of health care workers who did not become ill does not equal 60 for all items.

aAll variables have a P value of < .10 or were suggested by previous studies as potentially important.
b95% confidence interval about the odds ratio was calculated with test-based Mantel-Haenszel estimates about the odds ratio.
cLogit estimators of the 95% confidence interval use a correction of 0.5 to every cell of those tables that contain a zero.

tively, during the next 2 months. No other clustering of hepatitis A infections was noted at restaurants or other facilities in the county of origin during the period of the outbreak. Anti-HAV serology was obtained from the two donors reporting symptomatic illness coincident with the blood donations.

Characteristics of the Study Samples

Ninety-two percent (n = 132) of the questionnaires from potentially eligible controls (n = 154) were returned; all case subjects returned the questionnaire. Controls were required to be both serosusceptible (negative for total anti-HAV antibody) and to have returned the questionnaire (n = 91, Figure 3). The control group was further refined by limiting the group to the same job classifications (i.e., those with maximal patient exposure) as those of the health-care-worker case subjects (e.g., nurses, nursing assistants, nursing students, and ward clerks; n = 60). The reported rates of hand-washing after patient care, hand-washing after diaper changing, and wearing gloves when contact was anticipated with blood and body fluids or secretions were similar for both groups. After patient care, 82% of the case patients and 75% of the controls reported that they washed their hands routinely (relative risk [RR] = 1.09, 95% confidence interval [95% CI] = 0.77, 1.55). After diaper changing, 91% of the case patients and 100% of the controls reported always washing their hands (RR = 0.95, 95% CI = 0.85, 1.06). Similarly, 82% of the case and 63% of the control subjects reported consistent use of gloves when contact with blood or body fluids was anticipated (RR = 1.29, 95% CI = 0.85, 1.98).

Nursing assignments. The infection rates for nurses assigned to either patient were the highest during the exposure week of January 2 through January 8, 1990, just before the onset of symptoms in the father. During that week, the infection rates among nurses assigned to two or more shifts with the infant were higher than those for nurses assigned to a single shift (4 of 5 [80%] vs 1 of 6 [17%], respectively). Similarly, infection rates were higher for nurses assigned to two or more shifts with the infant’s father than for nurses assigned to a single shift (3 of 3 [100%] vs 1 of 13 [8%], respectively). The cumulative incidence risk ratio was elevated for nurses caring for either the infant (RR = 14.6, 95% CI = 3.4, 63.2) or his father (RR = 10.6, 95% CI = 2.2, 50.2) during that same week. The only two nurses assigned to care for both patients during the same week also became ill.

Risk-factor assessment. The univariate analysis (Table 1) identified the following significant risk factors for hepatitis A infection: eating on the ward (odds ratio [OR] = 14.2, 95% CI = 2.5, 80.5), bringing snack foods to share with others (OR = 8.8, 95%
CI = 2.4, 31.3), and providing hydrotherapy treatments (OR = 5.9, 95% CI = 1.3, 26.1). Of 12 different types of patient care given to adults or infants, none appeared to predispose workers to hepatitis A infection. No other risk factors (e.g., smoking, chewing on pens or pencils, eating specific snack foods at work, eating out with coworkers) were statistically significant risk factors. After correction for confounding variables with a stepwise logistic regression analysis, the single important risk factor for the development of infection was frequent eating on the ward (OR = 14.2, P = .0029). No additional variables met the criteria for retention in the model (P < .05) or improved the single variable model.

Discussion

Health care workers caring for thermally injured patients are potentially exposed to a variety of blood-borne pathogens daily through the open burn wounds that must be debrided with hydrotherapy and frequent dressing changes. In our burn treatment center, both case and control subjects reported a high level of prior compliance with routine hand-washing, glove use, and other barrier forms of universal precautions. Nevertheless, an important outbreak of hepatitis A occurred in a burn treatment center involving 11 health care workers and 1 patient with a secondary case. Once the epidemic was recognized, reemphasis of good hygienic and isolation practices and the administration of immunoglobulin apparently prevented other secondary cases. Although the relative contributions of each of these measures in terminating the outbreak cannot be assessed in the current study, we would recommend the use of a similar approach for control of a nosocomial outbreak.

We were unable to determine the source of hepatitis A infection in the two index patients. The usual incubation period of 10–50 days (mean = 1 month) is consistent with either nosocomial or community-acquired disease. The elevated cumulative incidence ratios among nurses exposed to either case in the week before onset of symptoms in the adult index patient suggest that both index patients were most infectious during that period, which corresponds to the time of greatest fecal shedding of hepatitis A virus. We also have epidemiologic evidence of an exposure dose–response relationship: the infection rates were higher for nurses assigned to more than one shift than for nurses assigned to only one shift with either patient and highest among nurses assigned to care for both patients. However, the infant son may have been infected before his arrival at the hospital, explaining the exposure to and timing of the disease in his father. Infants usually remain asymptomatic, liver enzymes may not be elevated, and secretion of virus in the stool may continue for weeks. Similar exposure dose–response relationships have been reported in the literature. In one multistate outbreak of 55 cases, the 16% infection rate among susceptible nurses was four times higher than that among physicians with considerably less exposure to case patients. Moreover, nurses working 12-hour shifts were significantly more likely to become infected than those working 8-hour shifts. In another epidemic, nurses assigned to two or more shifts with an infected infant with an ileostomy had an infection rate 4.6 times higher than those assigned to a single shift.

Because the index patients did not have direct contact with each other until after the onset of illness in the father, a nosocomial source for their infections appears unlikely. Nevertheless, a possible nosocomial source would be a contaminated blood product given to both patients. Transfusion-associated hepatitis in neonates has been recognized as the source of several nosocomial outbreaks involving health care workers. However, in our center, none of the donors gave blood to both patients. Moreover, of the 33 donors contributing blood to either patient, only 2 reported feeling ill near the time of their donation. Hepatitis A serologic tests from both of the latter donors were negative.

The outbreak occurred in the setting of a national increase in the incidence of hepatitis A in the United States. At the time of the outbreak, the incidence of community-acquired hepatitis A in the state of Iowa was fivefold higher than that in the previous year, with one fourth of the cases occurring in the same county of origin as the index cases.

Up to one third of community-acquired cases of hepatitis A have been linked to day-care centers. However, in our study, none of the children tested or family members of the babysitter from the small day-care home that had previously cared for the index infant were seropositive. Nevertheless, one of the six children cared for in the center could not be contacted for testing. Similarly, no apparent common source of exposure could be identified for the index family in the 2 months before admission.

A case–control study using seronegative, susceptible health care workers as controls convincingly demonstrated that frequent eating on the ward was the single most important risk factor for development of hepatitis A infection. Importantly, previous investigations of nosocomial outbreaks of hepatitis A have typically failed to implicate a particular mode of transmission. The finding that hepatitis A infection is clearly associated with eating on the hospital ward is not only biologically plausible, but also is entirely consistent with the acknowledged fecal-oral route of transmission of hepatitis A infections.

Our data indicating nonroutine hand-washing by approximately 25% of health care workers and nonroutine use of gloves by 37% of health care workers are self-reported, retrospective, and conservative estimates of compliance with standard hygienic procedures. These results support the previous findings of Rosenblum et al., who found a significantly increased risk of infection during an outbreak in a neonatal intensive-care unit among health care workers who did not wear gloves when taping an intravenous line.

We speculate that hygiene was suboptimal in the burn center before the outbreak and that hand contamination probably occurred. Hand contamination may have occurred after providing hydrotherapy (9 of 11 cases) or after other patient care activities. Subsequently, nosocomial infection likely occurred either through eating snacks or sharing food on the ward. The strategic placement of sinks at the entrance to the center may have resulted in improved hand-washing on leaving the burn treatment center and explain the lack of association of illness with eating in the hospital cafeteria. A food-related outbreak was also unlikely because there was geographic clustering of the cases on a single patient unit, serologic tests for hepatitis A among dietary workers were negative, and there was no supportive evidence in the case–control study. Importantly, none of the snack foods available on the center or the specific food items at the potluck dinner were associated with illness. However, we are unable to exclude absolutely the possibility that food contamination rather than, or in addition to, contamination of health care workers' hands was the apparent mode of transmission.

Previously reported outbreaks have been linked to patients with vomiting, diarrhea, or fecal incontinence. An out-
break of hepatitis A in a pediatric intensive-care unit in 1981 involving 10 secondary cases suggested that food was a potentially important risk factor. The apparent index patient in that outbreak had been incontinent of feces for several days before his death. His family had frequently brought in food that they shared with the boy and members of the staff. Sharing food with patients or their families, drinking coffee at work, sharing cigarettes, and eating in the nurses' office increased the likelihood of infection, although none of the variables reached statistical significance. Moreover, in another study, case patients were almost three times more likely to smoke than were controls (36% vs 13%), suggesting the importance of the fecal-oral route of transmission. Similarly, Rosenblum and colleagues reported that drinking beverages in the intensive-care unit was a significant risk factor for infection.

Recent data demonstrated that hepatitis A virus survives well on the fingerpads, despite drying, for 4 hours. Additionally, the virus was transferred effectively between fingerpads and from fingerpads to clean surfaces despite prolonged drying. After suspensions of the hepatitis A virus were dried for 20 minutes, an inoculum of the virus was transferred from an inanimate surface to the fingerpads. Both pressure and friction significantly increased the transfer of hepatitis A virus. The results of this experimental study support the importance of human hands in the direct spread of hepatitis A observed in the current outbreak.

The diagnosis of acute hepatitis A is usually confirmed easily by the presence of a positive IgM anti-HAV serologic test, which is typically positive very early in cases of acute infection. Four of our patients developed nausea, vomiting, and elevated alanine aminotransferase levels but were initially seronegative. Each of these case patients, however, developed IgM anti-HAV antibody over the next 5 to 7 days. Our findings confirm those of Zachoval and colleagues, who recently reported four patients with early acute hepatitis A infection who were initially seronegative for IgM anti-HAV antibody. Therefore, patients suspected of having early hepatitis A infection but who have a negative IgM anti-HAV test should have the test repeated several days later.

Our results confirm the empirical observations of Drusin and colleagues and Reed et al., and are consistent with previous guidelines suggesting that eating on the hospital ward when hygiene is suboptimal predisposes health care workers and patients to hepatitis A. Moreover, the combination of a low level of population immunity and an increase in the incidence of hepatitis A infection in the United States suggests that other hospitals may soon experience similar clusters of infection if health care workers continue to eat on the hospital ward.

Acknowledgments
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References