ABSTRACT. Objective. To elucidate virus spread from siblings with varicella to other family members and environmental objects in a family setting before and after onset of the disease.

Materials and Methods. Among a family consisting of five members, a boy developed varicella and the remaining two siblings developed the disease 17 and 18 days after onset of the index case. Swab samples from throats and hands of parents and three siblings and samples from several sources in the environment of the house were collected frequently before and/or after onset of the disease. Varicella-zoster virus (VZV) DNA in the samples was examined by a sensitive polymerase chain reaction amplification assay.

Results. In total, 108 samples from the throats and hands of the three children with varicella, 72 such samples from parents, and 72 samples from the surfaces of several sources in the house were collected. Eight days after onset of the index case (the older boy), VZV DNA was detected in both samples from the index case and on the surfaces of four sources (air conditioner filter, table, television channel push-buttons, and door handle), but not from the two other siblings or parents. Then, it was detected once on the mother’s hand and the air conditioner filter and three times on the television channel push-buttons by January 30, 1998, when the girl developed varicella, 17 days after onset of the index case. The younger brother developed the disease on January 31. Viral DNA could not be detected in any samples obtained on January 30; however, it was detected on the hands of the older boy and the father and in samples from the hand and throat of the girl on January 31. Thereafter, virus DNA was detected three times intermittently by February 13 on the hand and three times persistently in the throat of the girl. The virus DNA was detected three times between February 1 and 3 on the hand and three times between February 1 and 4 in the throat of the younger boy. It was detected occasionally on the hands of the older boy and the parents, and occasionally or intermittently on surfaces of four environmental sources between February 2 and 13.

Conclusions. The present study showed the rapid and broad contamination of the environment with the VZV DNA when the varicella patient appeared in a family, although it does not directly mean infectivity. Pediatrics 1999;103(5). URL: http://www.pediatrics.org/cgi/content/full/103/5/e61; varicella, varicella-zoster virus, transmission of VZV, VZV DNA, nested PCR.

ABBREVIATIONS. VZV, varicella-zoster virus; PCR, polymerase chain reaction.

Varicella (chickenpox) is a ubiquitous, contagious, generalized exanthematous disease of childhood, which is the result of primary infection of varicella-zoster virus (VZV). Epidemiologic and virologic observations suggest that the infection occurs after exposure to aerosolized VZV or by direct contact with patients with varicella or herpes zoster, although the mechanisms by which the virus is shed and spread to susceptible individuals are ill-defined. It is generally accepted that the typical case of varicella is infectious for 1 to 2 days before the appearance of rash and for 4 to 5 days thereafter. However, the period of virus excretion from patients with varicella is not well-understood. In this report, we examined virus spread from siblings with varicella to other family members and environmental objects in a family setting before and after onset of the disease using a sensitive polymerase chain reaction (PCR) amplification assay.

MATERIALS AND METHODS

The family examined in the present study consisted of five members: the father, age 36 years; mother, 36 years; older brother, 6 years; younger brother, 2 years; and sister, 5 years. They were all otherwise healthy before the present varicella episode and had no underlying diseases. The parents had a known history of varicella. The father was a staff member of the central laboratory facility of our university hospital. On the morning of January 13, 1998, the older brother developed vesicular rashes compatible with typical varicella accompanied by fever (number of skin lesions, 150–200; day and peak of fever, day 1 and 38.0°C; total days of illness, 5). The remaining sister (number of skin lesions, 25–50; total days of illness, 4) and younger brother (number of skin lesions, 50–75; total days of illness, 4) showed signs and symptoms of varicella without fever on January 30 and 31, 1998, 17 and 18 days after onset of the index case, respectively. All three were treated with routine doses of oral acyclovir (80 mg/kg/d in 4 divided doses) for 5 days started within 3 days after the onset of rash, and the girl at 1 day, and the younger boy at 1 day). Informed consent was obtained from the parents after the project was first thoroughly explained. The review board of our university for the study of human subjects approved the project of the present study.

Swab samples from throat and hand and samples from several sources in the environment of the house—including a door handle, table, television channel push-button, and air conditioner filter, collected by scrubbing the surface of the object using cotton swabs—were immersed immediately into sterile tubes containing 1 mL of Roswell Park Memorial Institute (RPMI)-1640. The sam-
varicella-zoster virus DNA could not be detected.

RESULTS

In total, 108 samples from the throats and hands of the three children with varicella, 72 such samples from parents, and 72 samples from the surfaces of several sources in the house were collected. Table 1 summarizes the results of the PCR assay. Eight days after onset of the index case (the older boy), VZV DNA was detected in both samples from the index case and on the surfaces of four sources (air-conditioner filter, table, television channel push-buttons, and door handle), but not from the other two siblings or parents. Then, it was detected once on the mother’s hand and the air conditioner filter and three times on the television channel push-buttons by January 30, 1998, when the girl developed varicella, 17 days after onset of the index case. The younger brother developed the disease on January 31. Viral DNA could not be detected in any samples obtained on January 30; however, it was detected on the hands of the older boy and the father and in samples from the hand and throat of the girl on January 31. Thereafter, viral DNA was detected three times intermittently by February 13 on the hand and three times persistently in the throat of the girl. The virus DNA was detected three times between February 1 and 3 on the hand and three times between February 1 and 4 in the throat of the younger boy. It was detected occasionally on the hands of the older boy and the parents, and occasionally or intermittently on surfaces of four environmental sources between February 2 and 13.

DISCUSSION

VZV is a highly contagious agent that leads to outbreaks of infection in closed populations. Transmission is thought to occur by aerosol spread, direct contact with an infected individual, or both. To identify the mode of transmission of VZV, it is important to isolate the virus from various samples obtained before and after onset of the disease. However, isolation of the virus from clinical samples other than vesicles is difficult and insensitive, so, instead, a sensitive PCR amplification assay was used in the present study. Consequently, positive PCR findings reflect the presence of VZV DNA but not necessarily the presence of infectious viral particles.

In the present study, the viral DNA could be detected in only 1 of 42 samples obtained during the 3 days before onset of the two secondary cases with

### Table 1

<table>
<thead>
<tr>
<th>Day of Sampling (in 1998)</th>
<th>Varicella-Zoster Virus DNA in Samples From Family Members and Surfaces of Several Sources</th>
<th>Development of Varicella</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand Throat</td>
<td>Hand Throat</td>
<td>Hand Throat</td>
</tr>
<tr>
<td>Boy, 6 Years</td>
<td>Girl, 5 Years</td>
<td>Boy, 2 Years</td>
</tr>
<tr>
<td>Jan 13</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Jan 21</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Jan 24</td>
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<td>—</td>
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<td>Jan 25</td>
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<td>Jan 30</td>
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<tr>
<td>Jan 31</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Feb 1</td>
<td>Yes</td>
<td>Yes</td>
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<td>Feb 2</td>
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<td>Feb 5</td>
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<tr>
<td>Feb 6</td>
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<tr>
<td>Feb 7</td>
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<td>—</td>
</tr>
<tr>
<td>Feb 13</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

* Samples from throats and other sources were collected by scrubbing the surface of the object with cotton swabs. Dashes indicate that varicella-zoster virus DNA could not be detected.
varicella. Although it is generally believed that the typical case of varicella is infectious for a few days before appearance of the rash, the actual amount of VZV excreted from the patients just before the onset may be smaller than expected. Alternatively it might have been possible to detect the viral DNA if a more sensitive PCR assay had been used in the present study. However, after the onset of the two cases with varicella, viral DNA was more frequently detected in cases and among family members and on the surface of several sources in the house. This finding would suggest that the amount of virus excreted from the patients during the eruptive stage is greater than that of the preeruptive phase of varicella. Of interest in understanding the pathophysiology and mode of transmission of varicella is that the virus DNA was detected occasionally or persistently or intermittently in family members and on several environmental surfaces for ~2 weeks after the onset of the disease. The positive finding in the throat of the two secondary cases during the acute stage of the disease indicates a possible source of transmission of the virus. This is further supported by a report in which higher amounts of viral DNA were detected in the saliva of all acute varicella patients tested during the first 3 days after onset. However, the positive findings detected in the convalescent stage of the disease might indicate the presence of VZV DNA but not the infectivity. Another interesting finding is the detection of viral DNA on the surface of the air conditioner filter. This evidence strongly suggests that transmission of the virus can occur by aerosol spread, because family members could not directly touch the filter. This is supported by the findings of Sawyer et al., whose PCR analysis of air samples from hospital rooms of patients with varicella revealed viral DNA in 82% of the samples 1.2 to 5.5 meters from the patient’s bed for 1 to 6 days after onset of rash. However, the significance of the positive findings other than in the throat of the two secondary cases with varicella, such as on the air conditioner filter, is not clear because the VZV DNA detected in these situations could represent noninfectious VZV DNA, and not viable virus particles. Levin et al. demonstrated that VZV could be recovered from a laboratory coat or human skin (0.1% to 0.3% of input VZV) or from a stethoscope (19% of input VZV) as late as 30 minutes after inoculation, suggesting the heat-unstable nature of the virus in the natural environment. Moreover, how long noninfectious VZV DNA can be detected by PCR is not clear. Although VZV has an extremely heat-unstable nature, comparison between the results of virus isolation and presence of VZV DNA by PCR is another important issue for future study. It is also of interest to determine the origin of the virus DNA detected by the present PCR assay. The virus is present in the fresh skin lesions, in upper and lower respiratory tract, and in other organs so that, theoretically, several routes would exist for dissemination of the virus. The relative role of airborne spread as contrasted with direct contact also remains unresolved.

Finally, because the three children with varicella in the present study were treated with routine doses of oral acyclovir for 5 days under the health insurance policy in Japan, the data obtained from this study should be compared with those from nontreated children.

ACKNOWLEDGMENTS

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## Spread of Varicella-Zoster Virus DNA to Family Members and Environments From Siblings With Varicella in a Household

Yoshizo Asano, Tetsushi Yoshikawa, Masaru Ihira, Hiroshi Furukawa, Kyoko Suzuki and Sadao Suga

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