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Prevalence of Enterovirus from Patients with Herpangina and Hand, Foot and Mouth Disease in Nagano Prefecture, Japan, 2007

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Based on the results of the National Epidemiological Surveillance of Infectious Disease (NESID) project in Nagano Prefecture, Japan, conducted from January to October 2007, this report describes epidemic trends for herpangina and hand, foot and mouth disease (HFMD). This report also refers to data provided by the Infectious Diseases Weekly Report (IDWR).

Herpangina patients were found in Nagano Prefecture beginning in the first week of the study. In the 27th week (July 2 - 8), the reported number of patients exceeded 1.0 case per sentinel, and in the 31st week (July 30 - August 5) the number reached a first peak of 5.16. Subsequently, the number decreased, then started to rise again. The 36th week (September 3 - 9) showed a second peak, of 3.84, so that the number of cases showed a bimodal pattern (Fig. 1).

From January to the end of October 2007, 26 samples of pharyngeal swabs were collected from herpangina patients at specially designated sentinel clinics, which were pathogen fixed-point medical institutions in Nagano Prefecture, for examination. For virus isolation, RD-18S, Vero9013, Vero, and HEP-2 cell lines were used, and the cultures were passed three times. For identification, neutralization tests using antiserum distributed by the National Institute of Infectious Diseases (NIID) and CF tests using suckling mice were conducted. Viruses were then isolated from all 26 samples. Eleven strains of coxsackievirus A5 (CA5), 9 strains of CA6, 3 strains of CA10, and 1 strain each of CA4, CA16, and human herpes simplex virus type 1 (HSV-1) were isolated (Table 1). These results suggested that CA5 and CA6 were the predominant pathogens of herpangina during this period in Nagano Prefecture. It has been known that the major virus for herpangina varied every year in Japan as well as in Nagano Prefecture. In this prefecture, the incidence rates of CA5 and CA6 were also high in 2005, and thus it was considered that herpangina caused by those viruses was epidemic after an interval of 2 years.

The weekly reported number of HFMD patients in Nagano Prefecture in 2007 increased slightly more slowly than the national average weekly rate. In the 28th week (July 9 - 15), the number exceeded 1.0 per fixed point, and in the 31st week (July 30 - August 5), a first peak of 2.53 was reached. This was followed by a decline, but in the 36th week (September 3 - 9) the number reached a second peak, at 1.87, thus showing a bimodal curve (Fig. 2).

From January to the end of October 2007, 24 pharyngeal swabs were collected from HFMD patients at specially designated sentinel clinics that are pathogen fixed-point medical institutions in Nagano Prefecture, and were then examined. Passage cultures were carried out using the above-mentioned culture cell lines for virus isolation, and neutralization tests using antiserum were conducted to identify viral strains. The culture fluid supernatant was examined by RT-PCR with primers EVP4 and OL68-1 to amplify a part (650 bp) of the VP4-VP2 region of enterovirus 71 (EV71) if necessary. Furthermore, the results were confirmed by nested-PCR with EV71 primer pairs. Viruses were then isolated from 15 speci-
Twelve strains of CA16, 3 strains of EV71, and 1 strain of CA6 were identified. These results suggested that one HFMD patient was infected with both EV71 and CA16.

In Nagano Prefecture, a high percentage—93.8% (15/16)—EV71 was isolated from HFMD patients in 2006, so we here focused on the next year. However, the major causative agent was CA16 in the 2007 study period (Table 1). With reference to the Infectious Agents Surveillance Report (IASR) published on October 31, 2007, the results were compared with isolated virus detection results across Japan. In 2007, CA16 was detected in large numbers all over the country. It is thought that the results in Nagano Prefecture are similar to the national results.


<table>
<thead>
<tr>
<th>Case</th>
<th>No. of specimens</th>
<th>CA4</th>
<th>CA5</th>
<th>CA6</th>
<th>CA10</th>
<th>CA16</th>
<th>EV71</th>
<th>HSV-1</th>
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<tbody>
<tr>
<td>Herpangina</td>
<td>26</td>
<td>1</td>
<td>11</td>
<td>9</td>
<td>3</td>
<td>1</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>HFMD</td>
<td>24</td>
<td>–</td>
<td>–</td>
<td>1</td>
<td>–</td>
<td>12</td>
<td>3</td>
<td>–</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>1</td>
<td>11</td>
<td>10</td>
<td>3</td>
<td>13</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

HFMD, hand, foot and mouth disease; CA, coxsackievirus; EV, enterovirus; HSV, herpes simplex virus.