A variety of respiratory viruses found in symptomatic travellers returning from countries with ongoing spread of the new influenza A(H1N1)v virus strain

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Clinical specimens from 79 symptomatic individuals with a recent history of travel to countries with verified transmission of influenza A(H1N1)v (North America) were tested with a multiple real-time PCR targeting a broad range of agents that may cause acute respiratory infection. This analysis revealed that besides four cases of influenza A(H1N1)v, other respiratory viruses were diagnosed in almost 60% of the samples. These observations are a reminder that many different viral transmissions occur simultaneously in countries with ongoing spread of influenza A(H1N1)v. The findings demonstrate that the definition of suspected cases by clinical and epidemiological criteria has only a poor capacity for discriminating influenza A(H1N1)v from other viral infections.

Background
A new influenza A(H1N1)v variant has spread globally since its first appearance in April 2009 [1,2] and as of 17 June 2009 there were 39,620 cases reported by the World Health Organization (WHO) [3]. On 30 April 2009, the European Commission suggested a case definition [4], which has been adopted and modified by most authorities in the European Union Member States. In agreement with this recommendation, testing for influenza A was recommended in Sweden for cases with a clinical presentation including respiratory symptoms and fever above 38°C, and epidemiological circumstances such as recent travel (within seven days) to areas where the new influenza has been observed [5] or close contact with confirmed cases.

The regular sentinel surveillance for seasonal influenza has been extended and now focuses on identification of imported cases with influenza A(H1N1)v, and on preventing secondary transmission by contact tracing and antiviral medication in an attempt to delay sustained community transmission. In order to provide a better basis for the decision whether or not to initiate preventive measures, expanded testing, targeting a broad range of respiratory agents, has been applied to specimens from all suspected cases in the region Västra Götaland (1.5 million inhabitants). We report here the results of this expanded testing.

Material and methods
This report includes samples of patients who, during the period from 24 April to 10 June 2009 presented with influenza-like symptoms and a history of recent travel to the United States or other countries with ongoing influenza A(H1N1)v transmission. The test performed was a multiple real-time PCR targeting a broad range of agents. The results of the analysis are summarized in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Viral aetiology</th>
<th>Number</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhinovirus</td>
<td>28*</td>
<td>34</td>
</tr>
<tr>
<td>Coronavirus</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Influenzavirus B</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Human para influenza virus (1-3)</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>2*</td>
<td>2</td>
</tr>
<tr>
<td>Influenzavirus A(H1N1)v</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Metapneumovirus</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Enterovirus</td>
<td>1*</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory syncytial virus</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae, Chlamydia pneumoniae</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Negative</td>
<td>32</td>
<td>39</td>
</tr>
<tr>
<td>Total number</td>
<td>82*</td>
<td>100</td>
</tr>
</tbody>
</table>

* Three patients had double infections with rhinovirus together with enterovirus, metapneumovirus or adenovirus.
is likely to be underestimated, because only the severe cases are
reported. This illustrates a dilemma that the criteria for suspected
cases of influenza A(H1N1)v are relevant as indicators of a viral
infection, but not specific for rhinovirus was helpful for the decision not to treat the patient of
some cases the identification of an alternative aetiology such as
PCR. In cases that presented with typical influenza-like symptoms
as confirmation for the result of the first, general influenza A
in some cases the criteria for suspected cases of influenza A(H1N1)v are
relevant as indicators of a viral infection, but not specific for
influenza A. On the other hand, applying more restrictive criteria
would probably have excluded most infections with the new
A(H1N1)v strain, considering that their clinical presentation has
been reported to be relatively mild. This illustrates a dilemma
with surveillance actions aiming at revealing the spread of new
respiratory infections will be due to influenza A virus. The value
of broad virology testing decreases in the course of an influenza
epidemic, when the detection rate of other aetiologies may decrease
from above 50% as observed in this report to below 10% during
the influenza peak (unpublished observations from our laboratory).

The cases with influenza A were analysed further by a typing
PCR that within 4-5 hours could identify whether the strain was
a traditional H1N1 or H3N2 virus, or the new H1N1 variant. This
typing system targets specific regions of the haemagglutinin gene
and has been developed in our laboratory (unpublished). It has
proved to have a good sensitivity, as illustrated by cycle threshold
(CT) values that are typically lower than those obtained in the
general PCR for influenza A, which targets a conserved region of
the matrix protein gene.

The results of the multiple PCR used in our setting were
available within 24 hours after sampling and served at the same
time as confirmation for the result of the first, general influenza A
PCR. In cases that presented with typical influenza-like symptoms
but were negative for influenza A in the first PCR, the finding of
an alternative aetiology was helpful for the decision to refrain from
preventive measures. Such measures include oseltamivir treatment
of patients and influenza testing and prophylactic treatment of their
close contacts. The clinical practice was not always different, but
in some cases the identification of an alternative aetiology such as
rhinovirus was helpful for the decision not to treat the patient of
contacts, even when the patient had symptoms clearly indicative of
possible influenza. From this experience we therefore conclude that
a broad diagnostic test is a valuable tool in the early investigation of
a new emerging respiratory virus like the new influenza A(H1N1)v.

Note added in proof:
On 17 June, Sweden changed to a stricter case definition for suspected
cases. It now requires more than two symptoms besides epidemiology
and fever.

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