Experience With the Rapid Directigen Test for Influenza

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Objective: To determine the sensitivity and positive predictive value of the Becton-Dickson Directigen AB performed on-site in a nursing home compared to viral culture.

Setting: A 721-bed skilled nursing facility for veterans and spouses.

Design measurements: Nasopharyngeal specimens were obtained with a low clinical threshold from residents during 3 influenza seasons for rapid antigen testing in the nursing home. The specimens were then transported for viral culture by courier on ice to a laboratory 45 miles away.

Results: A total of 327 samples were obtained; 36 were positive for influenza A by rapid test, and all but 2 grew the organism on tissue culture with a positive predictive value of 94%. Nineteen specimens were negative by rapid test, but grew influenza A on tissue culture with a sensitivity of 64%. Influenza prophylaxis was usually initiated the day the first positive rapid test was encountered when influenza was active in the community.

Conclusion: The Directigen AB is a reliable indicator of influenza when influenza has been culture-confirmed in the community. Although sensitivity is limited, a group of rapid tests provided early laboratory confirmation and facilitated the application of prophylaxis. (J Am Med Dir Assoc 2006; 7: 37–39)

Keywords: Influenza; prophylaxis; nursing home; rapid test

During an explosive outbreak, brief delays in starting influenza prophylaxis could expose many residents to a potentially fatal illness.1,2 Unfortunately, identification of influenza on clinical grounds is complicated by overlapping respiratory pathogens such as respiratory syncytial or parainfluenza virus, as well as aspiration events.3 The standard clinical case definition for influenza lacks proven sensitivity in vaccinated residents of long-term care facilities.4 A previous review of 154 culture-confirmed cases revealed that 19% never had a temperature higher than 99.5°F recorded at any time during their illness, including 5 of 19 with infiltrates.5 Therefore, we had a low “clinical” threshold for collecting nasopharyngeal specimens. No temperature threshold was required.

Currently, the Centers for Disease Control and Prevention (CDC) recommends that chemoprophylaxis be based on laboratory confirmation of influenza. However, to avoid delays, “treatment and chemoprophylaxis should be initiated if influenza is strongly suspected and test results are not yet available.”6 In a previous publication entitled, “Delays in the Application of Outbreak Control Prophylaxis in a Nursing Home,” we identified the average 4-day delay between specimen acquisition and culture confirmation as a principal factor in such delays.1 Rapid diagnostic tests performed on site could quickly confirm the presence of influenza. Nasopharyngeal specimens are usually preferred because of higher quantities of detectable virus.7 We report our experience with a rapid diagnostic test during 3 influenza seasons. Unlike our previous reports, which included intense clinical surveillance by skilled research nurses, this report includes surveillance performed as standard practice.1–3,5

METHODS

The Wisconsin Veterans Home is a skilled nursing home for veterans and their spouses, administered by the State of Wisconsin. During this report, the average daily census was 721. Seventy-nine percent of residents were male with a mean age of 74 ± 10 years with an average annual mortality of 19% and 239 hospitalizations per year. The Home has 4 nursing buildings and a separate activity building for all residents. The 4 nursing buildings contain 14 floors. During the influenza seasons included in this report, 87% of all residents and 41%
of nursing staff, respectively, were vaccinated with the commercially available trivalent influenza vaccine.


The following information was available for nursing staff in our policies and procedures to guide specimen collection during the period of influenza activity in the community:

"Influenza may present atypically in the elderly (ie, falls, confusion, or increased dependency). All cases must have a new respiratory illness with lower respiratory signs and symptoms including cough, congestion or abnormal sounds in the chest, or, upper respiratory signs and symptoms including rhinorrhea, congestion or sore throat. Systemic signs and symptoms are strongly supportive of the presence of influenza. The most significant include fever, headache, myalgia, malaise, anorexia, abnormal vital signs including heart rate >100, respiratory rate >25, or deterioration in oximetry, deterioration in activities of daily living or mentation (delirium)" (Wisconsin Veterans Home Policies and Procedures).

This approach to case finding is admittedly controversial and not validated. Sampling was usually suspended for at least 5 days after prophylaxis was initiated.

The Directigen test was performed in the Home's laboratory within 1 hour of specimen collection. All specimens were transported in viral media on ice by courier and inoculated into cell cultures within 36 hours of collection. Our study was laboratory-based. We did not obtain signed informed consent to report personal, protected medical information and cannot report detailed information about the clinical characteristics of all residents who were sampled.

RESULTS

A total of 327 Directigen AB samples were collected by swab from the nasopharynx to track the spread of influenza within our facility. Only 36 rapid diagnostic tests were positive for influenza A, and all but 2 grew the organism on tissue culture, with a positive predictive value of 94% versus culture (Table 1).

An additional 19 specimens were negative with the rapid diagnostic test, but subsequently grew influenza A on tissue culture, resulting in a sensitivity of 64% versus culture. Finally, 272 specimens were negative for influenza by both rapid test and cell culture yielding a specificity of 99% compared to culture.

DISCUSSION

Our experience indicates that a positive Directigen AB rapid test is a reliable indicator of influenza during the influenza season. False positive rapid diagnostic tests have been reported so that initial community cases identified by rapid diagnostic test should be confirmed by culture. Monto et al8 also performed the Directigen AB test and culture on nursing home residents during the 2001–2002 influenza season including 18 positive rapid tests (13 with positive cultures, 5 with negative cultures). The sensitivity of the rapid test versus culture was 76% versus culture. Specimens for rapid diagnostic tests were obtained from the throat (versus nasopharynx) and transported without being placed in viral transport media, which might have compromised the ability to detect the organism. The manufacturer recommends transport in liquid media.

Walsh et al9 reported that rapid antigen detection with the influenza A Directigen (Becton-Dickson, Cockeysville, MD) (versus A and B in our study) was positive in 14 of 29 hospitalized elderly in whom virus was isolated in cell culture and in 12 culture-negative subjects. The sensitivity of Directigen A was 48% compared with culture. Leonardi et al10 also used the Directigen for Influenza A with a sensitivity of 87% in 46 institutionalized geriatric patients with positive cultures.

A pooled analysis of zanamivir treatment studies that included culture, polymerase chain reaction (PCR), and serology in 791 symptomatic cases (laboratory-confirmed by at least 1 method, mean age 36) found that only 74% of cases included a positive culture.11 Monto et al8 performed both PCR and culture on specimens from 83 nursing home residents during the 2001–2002 season. All 17 with positive cultures had positive PCR. Of interest, there were 27 with negative cultures and positive PCR. Therefore, if PCR was the gold standard, the sensitivity of culture was only 39%. Given the sensitivity limitations of both rapid tests and cultures, we would not recommend withholding antiviral treatment in an individual with a compatible syndrome during a period of influenza activity on the basis of a negative rapid diagnostic test. Current CDC publications cite the sensitivity of rapid diagnostic tests as approximately greater than 70% and approximately greater than 90% specific compared to viral culture.1 The rapid test used in our study is not Clinical Laboratory Improvement Amendment–waived and is considered to be moderately complex requiring specific laboratory certification. The Quick Vue influenza test (Quiedil, San Diego, CA) and ZstatFlu (ZymeTx, Inc, Oklahoma City, OK), however, is a Clinical Laboratory Improvement Amendment–waived test that may be done in any health care setting.12

Although the sensitivity of the rapid diagnostic test is limited, we found that a group of rapid tests performed on symptomatic individuals was helpful in the early identification of influenza and the application of antiviral prophylaxis. Prophylaxis would have been delayed at least 3 to 4 days if we had waited for the culture report. In our experience, rapid diagnostic tests are useful to confirm influenza in a building using grouped data, but should not be relied upon for management of individual residents. Only 17% of the specimens

### Table 1. Distribution of Rapid Test and Viral Culture Determination

<table>
<thead>
<tr>
<th>Culture-Positive</th>
<th>Culture-Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid test–positive</td>
<td>34</td>
<td>2</td>
</tr>
<tr>
<td>Rapid test–negative</td>
<td>19</td>
<td>272</td>
</tr>
<tr>
<td>Total</td>
<td>53</td>
<td>274</td>
</tr>
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we collected (55 of 327) yielded any laboratory confirmation of influenza. Undoubtedly, all cases of influenza among the 327 subjects were not identified. It is likely that a higher proportion of specimens would produce positive results if we required a temperature threshold of 99.5 to 100°F prior to sampling. However, in an earlier study, approximately 20% of culture-confirmed cases did not have a temperature higher than 99.5°F recorded at any time during their illness.5

There is no established threshold for initiating “outbreak” control prophylaxis in a nursing home. Monto et al8 recently recommended prophylaxis “when 2 cases of laboratory-confirmed influenza illness were detected in a nursing home within 5 days.” A CDC publication, “Influenza Outbreaks in Acute Care Facilities” provides 2 threshold levels.12 The first is clinical, “a cluster of 3 or more patients with nosocomial-acquired clinically suspected influenza-like illness identified on the same floor within 3 days. The second, “1 or more patients with nosocomial-acquired laboratory-confirmed influenza.”12 Following outbreak identification, chemoprophylaxis should be administered to all residents regardless of influenza vaccination and continued for a minimum of 2 weeks or approximately 1 week after the last case.13 The decision to initiate influenza prophylaxis in a nursing building should optimally be made prior to the development of a full-blown clinical outbreak.5 Factors to consider include the following:

1. Number and clustering of laboratory-confirmed cases within the facility. (Clustering implies transmission within the facility.)
2. Pattern of new clinical respiratory illnesses, clustered, severe cases demanding prophylaxis more than sporadic mild cases.
3. Quality of the match between the circulating and vaccine strain.1
4. Level of community influenza activity.
5. Severity of outbreaks in nursing homes affected earlier in the season.1

I generally initiated prophylaxis on the day influenza was confirmed by rapid test if influenza-like illness was prevalent in the surrounding community. The reader is referred to previous publications for a more complete discussion of influenza chemoprophylaxis.1,14

REFERENCES