

MMWR-EVALUATION OF RAPID INFLUENZA DIAGNOSTIC TESTS

**Key Messages prepared by:
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SUMMARY

The August 6, 2009 *Morbidity and Mortality Weekly Report* article, “Evaluation of Rapid Influenza Diagnostic Tests (RIDT) for Detection of Novel Influenza A (H1N1) Virus—United States, 2009” evaluates three commercially available rapid influenza diagnostic tests (RIDTs) for their ability to detect novel influenza A (H1N1). RIDTs from three companies were reviewed and results indicate that these tests can detect novel influenza A (H1N1) in respiratory specimens, but the overall sensitivities range from 40-69% meaning that many influenza infections will be missed. Given the lower sensitivities found with RIDTs compared to rapid reverse transcriptase-polymerase chain reaction (rt-PCR), decisions regarding treatment and further testing among patients with negative results from RIDT testing should be based upon clinician suspicion, underlying medical conditions, severity of illness, and risk for complications in those persons suspected of having novel H1N1 virus infection. Early treatment with influenza antiviral medications of persons infected with influenza who are at increased risk of influenza complications and those people hospitalized with suspected influenza is important to maximize benefit of treatment and to lessen the severity of illness.

POINTS FOR CONSIDERATION

- Rapid Influenza Diagnostic tests (RIDTs) are tests that detect influenza A or B antigens and can provide results within 15 minutes.
- In this study, RIDTs from three companies were reviewed for their ability to detect influenza A viral antigens in selected original clinical samples submitted to CDC that tested positive for novel influenza A (H1N1), seasonal influenza A (H3N2), or seasonal influenza A (H1N1) viruses.
 - Sixty-five (65) original clinical samples were used for testing. Of those, 45 were positive for novel influenza A (H1N1), five samples were positive for seasonal influenza A (H1N1), and 15 samples were positive for seasonal influenza A (H3N2) by CDC rRT-PCR.
- The study found that commonly used RIDTs are capable of detecting novel influenza A (H1N1) from respiratory samples containing high virus titers, but sensitivities declined substantially as cycle threshold (Ct*) values increase.
 - * Cycle threshold (Ct) values are indicators of the amount of virus in a sample. Lower cycle threshold values indicate higher amounts of viral material in the specimen.
- The overall sensitivity of RIDTs to detect novel influenza A (H1N1) was less than 70% among all samples tested, with a range from 40-69%.
 - The overall sensitivity was determined by the percentage of test positive samples versus all clinical materials positive for this virus by rRT-PCR.

- Overall sensitivity to detect novel influenza A (H1N1) was 69% for QuickVue A+B; 49% for Directigen EZ; and 40% for BinaxNOW.
- All RIDTs performed well compared to rRT-PCR for samples with cycle threshold (Ct)* values less than 20 with 89-100% sensitivity.
 - Sensitivities of the RIDTs was highest among specimens with Ct values of <20.
 - Among samples with Ct values of 20 or greater, the sensitivity declined substantially.
- Given the lower sensitivity of RIDTs compared to other assays, such as rRT-PCR, clinicians should understand that a negative result by RIDT does not exclude influenza virus infection.
 - Decisions regarding treatment and further testing among patients with negative results from RIDT testing should be based upon clinician suspicion, underlying medical condition, severity of illness, and risk for complications in those persons suspected of having novel H1N1 virus infection.
- The findings from this study are similar with other recent studies, which reported that the sensitivity of some RIDTs to detect novel influenza A (H1N1) in clinical specimens ranged from 10-51% compared with rRT-PCR.
- CDC's guidance on interpretation of RIDTs for testing of patients with suspected novel H1n1 virus infection is available at http://www.cdc.gov/h1n1flu/guidance/rapid_testing.htm

BACKGROUND ON RIDTs

- RIDTs may be referred to as “point-of-care” tests because they provide results quickly enough to inform clinical decisions during a patient’s office visit.
 - A positive test means that influenza infection is likely and can inform influenza treatment decisions by providing influenza type (A vs. B).
- RIDTs vary in their capacities to detect influenza. For instance some can detect and distinguish between influenza A and B, others can detect but not distinguish between influenza A and B, and some can only detect influenza A.
- RIDTs do not distinguish between influenza A subtypes and cannot provide information about antiviral drug susceptibility.
- The sensitivities of RIDTs depend on multiple factors including virus type (A or B), subtype of influenza A, quality of specimen collection and handling, type of specimen collected, age of the patient, and time from illness onset to specimen collection.
- Due to the limited sensitivities of RIDTs to detect influenza, interpretation of the test results should be done with care as false negative results are common.

QUESTIONS & ANSWERS

What RIDTs were used for this study?

This study used the Inverness Medical BinaxNOW[®] Influenza A&B (Binax, Inc. Scarborough, Maine), Becton Dickinson Directigen[™] EZ Flu A+B test (Becton, Dickinson and Company, Sparks, Maryland) and Quidel QuickVue[®] Influenza A+B (Quidel Corporation, San Diego, California).

How were the RIDTs chosen for this study?

The RIDTs used in the study were chosen as they are the three most widely used FDA-approved RIDTs in the United States at this time. Other RIDTs are currently being evaluated using the same methodology.

Are there plans to conduct further testing with more RIDTs and more specimens?

There are plans to test more novel H1N1 flu, seasonal H3N2 flu and seasonal H1N1 flu samples and negative samples. All three RIDTs tested for this study will be a part of the continuing evaluation. Additional FDA-approved RIDTs will also be included in this study.

What do the results of this study mean for clinicians using RIDTs to detect novel influenza A (H1N1)?

RIDTs can provide useful information that might impact patient care; however the tests have limitations. While the findings from this study indicate that RIDTs can detect novel influenza A (H1N1) in respiratory specimens, given the overall sensitivities found, many infections will be missed and false negatives may occur.

For instance, a negative RIDT result does not necessarily exclude influenza virus infection. For those patients that test negative by RIDT a diagnosis of influenza should still be considered if they have influenza-like symptoms. Decisions regarding treatment and further testing among patients with negative results from RIDT testing should be based upon clinician suspicion, underlying medical conditions, severity of illness, and risk for complications in those persons suspected of having novel H1N1 virus infection. Early treatment with influenza antiviral medications of persons infected with influenza who are at increased risk of influenza complications and those people hospitalized with suspected influenza is important to maximize benefit of treatment and to lessen the severity of illness.