

# Reporting, Reliability and Interpretation of Rapid Influenza Test Results

## Introduction

The novel H1N1 influenza is continuing to spread in Nevada, nationwide and around the globe. There are no signs of cases tapering off, and so far the virus has not changed much since it crossed the species to humans. Nevada is still experiencing a steady increase in the number of cases and as of today there were more than 320 confirmed, 20 who required hospitalization (most of those had pre-existing conditions) and two fatal cases.

This newly emerging H1N1 virus is now making up more than 99% of all the typed laboratory isolates tested in Nevada and the U.S. More than 76% of all cases were among individuals younger than 24 and about 99% were among individuals age 64 years or less. Nearly 80% of all who required hospitalization were younger than 50 years of age.

At this point of the pandemic we are focusing our surveillance efforts in order to gain more information about severe outcomes of H1N1 infections (such as those observed among hospitalized or deceased cases). The Nevada State Health Division and the Centers for Disease Control and Prevention (CDC) continue to receive anecdotal reports of false positive and false negative influenza A rapid test results. Clinicians are urged to test individuals for the novel influenza (H1N1) virus if they have an acute febrile respiratory illness or sepsis-like syndrome. Certain groups may have atypical presentations including infants, elderly and persons with compromised immune systems. Priority for testing includes persons who require hospitalization, present with severe influenza infection or are at high-risk for severe disease.

Some commercially available rapid tests can distinguish between influenza A and B viruses. However, these tests have suboptimal sensitivity to detect seasonal influenza viruses with an unknown sensitivity and specificity to detect human infection with novel influenza A (H1N1) virus. Immunofluorescence (DFA or IFA) assays depend upon the quality of clinical specimens, operator skills, and similar to rapid tests have unknown sensitivity and specificity to detect human infection with novel influenza A (H1N1) virus in clinical specimens. Therefore, a negative rapid tests or immunofluorescence assays could be falsely negative and should not be assumed as final diagnostic tests for novel influenza A (H1N1) virus infection. On the other hand isolation of novel influenza A (H1N1) virus is diagnostic of infection, but viral cultures may not yield timely results for prompt clinical management.

Rapid flu tests could be unreliable and providers are urged to perform a reverse-transcription polymerase chain reaction (RT-PCR) test for all hospitalized and/or severe cases of influenza like illnesses (ILI).

## Reporting

Patients meeting the following criteria should be reported to local health departments or the Nevada State Health Division: All patients being admitted or currently hospitalized with acute febrile respiratory illness, including:

- Fever >100.4° F or 38.0 C° and ILI, Acute Respiratory Distress Syndrome (ARDS), pneumonia or respiratory distress who test positive for influenza A
- Critically ill hospitalized patients (e.g., on a ventilator) with acute respiratory symptoms in whom there is a strong suspicion of influenza, regardless of influenza rapid test results

Routinely the following conditions are reported to local health authorities:

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- Pediatric death with clinically compatible illness in which there is a positive influenza test
- Sudden pediatric death from unknown cause, but thought to be due to natural causes
- Pediatric death from unknown, febrile respiratory illness

In the current pandemic of the novel H1N1 influenza virus, it is helpful to have healthcare providers reporting also the following additional events:

- All unexplained deaths involving febrile respiratory illness
- All deaths among persons confirmed to have novel H1N1 influenza virus

Furthermore, it is strongly advisable that healthcare providers notify local or state health authorities of any fatality that occurs among patients diagnosed with novel H1N1 influenza, even if they were previously reported as suspected, probable or confirmed cases. Additionally, the Nevada State Health Division asks medical providers to consider the diagnosis of novel H1N1 influenza in any fatal cases of unexplained acute febrile respiratory illness, regardless of age.

### **Reliability of Rapid Testing for the Novel Influenza A (H1N1) Virus**

The reliability of rapid influenza diagnostic tests depends largely on the conditions under which they are used and are entirely based on the experience with seasonal influenza. For the detection of seasonal influenza virus infection, and when compared with the viral culture or RT-PCR the *sensitivity* of rapid diagnostic tests ranges from 50 to 70%, while *specificity* of rapid diagnostic tests for influenza ranges between 90 to 95%. However, it is important to keep in mind that the sensitivity and specificity of these tests for detection of the novel H1N1 flu virus is currently unknown. False-positive and true-negative results are more likely to occur when influenza is uncommon in the community, which is generally observed at the beginning and end of an outbreak. However, false-negative and true-positive results are more likely to occur when influenza is common in the community that is typically at the height of an outbreak (i.e. this current pandemic). Additionally, test sensitivity may vary depending on when, in the course of illness, the specimen was collected. Respiratory specimens for testing are best when collected in the first four to five days of illness and viral shedding is greatest.

Given these limitations, the decision of whether or not to test patients with rapid influenza diagnostic tests should be based upon the patient's presenting symptoms, and/or the patient's risk for severe disease or other complications.

### **Interpretation of Rapid Testing for the Novel Influenza A (H1N1) Virus**

A patient testing positive for influenza B by rapid diagnostic test is likely to have been infected with seasonal influenza B virus that is continuing to circulate or it could be a false-positive result. Such patients are unlikely to have novel H1N1 virus infections, but they may.

If a patient tests positive for influenza A by rapid antigen she/he may have one or more of the following:

- Novel H1N1 virus infection
- Seasonal influenza A virus infection
- A false positive test result

Severe cases that test positive on a rapid influenza antigen test need additional testing, and can be treated empirically with antiviral medications if clinically indicated. Please see CDC *Guidance on Antiviral Recommendations for Patients with Novel Influenza A (H1N1) Virus Infection and Their Close Contacts* at <http://www.cdc.gov/h1n1flu/recommendations.htm>. Nasopharyngeal swab/aspirate or nasal aspirate should be collected and sent to the state public health laboratory for RT-PCR to determine if the patient has H1N1

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infection, seasonal influenza A virus infection or a false-positive test result. Please see CDC *Guidelines for Specimen Collection and Interim Bio-safety Guidelines for Laboratory Workers*.

If the patient with respiratory illness has an epidemiologic link to a confirmed case (i.e. had close contact with a confirmed case) and the rapid antigen test was negative for influenza, further testing and treatment should be based upon clinical suspicion, severity of illness, and risk for complications. If there is no epidemiologic link and the patient has mild illness; further testing and treatment are not recommended.

## Summary

During this unusual and extended influenza season we are currently experiencing, all hospitalized patients with acute febrile respiratory illness (documented fever  $>100.4^{\circ}$  F or  $38.0^{\circ}$  C and ILI, ARDS, pneumonia or respiratory distress) should be presumed to have influenza; may require timely testing and empirical treatment with antiviral therapy until proven otherwise. Such severe cases should be reported to local health departments or the Nevada State Health Division without delay.

Rapid influenza diagnostic tests can help in the diagnosis and management of patients who present with signs and symptoms compatible with influenza. However, rapid influenza tests may be unreliable. Clinicians may consider using rapid diagnostic tests as part of their evaluation of patients with signs and symptoms compatible with influenza, but results should be interpreted with caution.

A negative rapid test does not exclude infection with novel influenza A (H1N1) virus. Confirmation of novel H1N1 flu infection can only be made by reverse-transcription polymerase chain reaction (RT-PCR) or viral culture. RT-PCR is the recommended test for confirmation of novel influenza A (H1N1) cases and is available at the Nevada State Public Health Laboratory.

For additional information on the novel influenza H1N1 pandemic in Nevada, the United States and globally, see the Nevada State Health Division's website at <http://health.nv.gov/>, CDC website at [www.cdc.gov/h1n1flu/](http://www.cdc.gov/h1n1flu/) and the World Health Organization (WHO) website at <http://www.who.int/csr/disease/swineflu/en/index.html>.

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