Rapid Influenza Diagnostic Tests Used as Screening Tools During an Outbreak of the 2009 Novel Influenza Virus: The Nebraska Experience

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The NPHL performs influenza surveillance testing to support the Nebraska Department of Health and Human Services (NE-DHHS). For the 2008-09 season, surveillance testing at the NPHL was performed using a Food and Drug Administration (FDA)-cleared Luminex xTAG Respiratory Viral Panel (RVP) assay (Luminex Molecular Diagnostics, Toronto, Canada). This assay identifies 11 upper respiratory viruses to include adenovirus, respiratory syncytical viruses (RSV) A and B, parainfluenza viruses 1 - 3, human metapneumovirus, rhinovirus, and influenza A virus /H1, A/H3 virus, and influenza B virus. Year-round surveillance activity in Nebraska includes testing of specimens received from sentinel physician clinics, hospitals, and reference laboratories. These facilities utilize a variety of commercially available CLIA waived rapid influenza diagnostic tests (RIDTs) that distinguish and differentiate between influenza A and B viruses.

On April 22nd, the Centers for Disease Control and Prevention reported that a novel strain of influenza A virus(hereafter called the 2009 H1N1 variant strain [H1N1v]) was identified in California and traced to a point-source in Mexico**[1]**. In preparation for the anticipated increased testing demands, the NPHL and the Nebraska Department of Epidemiology decided to restrict samples to optimize testing. The testing algorithm included the evaluation of clinical specimens from patients meeting the following conditions: 1) RIDT-positive with travel history to Mexico or having an exposure to someone that had traveled there or 2) known travel history to Mexico or had an exposure to someone with travel history and were symptomatic but RIDT-negative.

During the 5-week outbreak period, 5,730 RIDTs were reported by local hospitals, reference labs, and physician clinics throughout the state. Of these, 255 were positive for influenza A virus, 150 were positive for influenza B virus, and 8 were reported as positive for influenza virus but not differentiated. From the RIDTs performed state-wide, 336 specimens underwent further diagnostic testing at the NPHL for H1N1v. They consisted of 234 (69.6%) RIDT-positive and 102 (30.4%) RIDT-negative specimens from the following test kits: Inverness Medical BinaxNOW Influenza A&B (150 specimens; 44.6 %), Meridian TruFlu (44 specimens; 13.1%), Quidel QuickVue Influenza A&B (92 specimens; 27.4%), and Remel Xpect Flu A&B (50 specimens; 14.9%).

Testing at the NPHL showed that the distribution of influenza viruses detected among RIDT and RVP influenza-positive specimens was roughly equivalent for seasonal influenza viruses (A/H1, A/H3 and B) and the H1N1v strain. While the combine sensitivity of all RIDTs was 97.69%, the overall specificity (i.e. true positives) of the RIDTs for influenza viruses was low at 48.05%. Of the 102 RITD-positive and RVP influenza-negative specimens, 55 were negative for any virus while 47 specimens were positive for other upper respiratory viruses by the RVP test: rhinovirus (28), adenovirus (5), parainfluenza viruses (13), and RSV (1).

In conclusion, an overall marked difference in the performance between types of RIDTs was varied. The Xpect Flu kit was associated with more discrepant results (74%) than the other RIDTs (BinaxNOW 29%; TruFlu 34%; and QuickVue 16%). Additionally, a difference in the rates of discrepancies by type of test facility was observed. Hospitals had a higher proportion of discrepant results compared to doctor offices (40% vs. 19%). Some facilities using one type of kit had 100% agreement with the Luminex xTAG RVP while other facilities using the same kit had less than 25% agreement. Factors that could account for the low levels of specificity and the

agreement rates include variations in: 1) specimen collection and transport, 2) specimen collection material used, 3) testing techniques, and 4) subjective interpretation of the lateral-flow immunodiagnostic solid-phase RIDT results to observe whether or not a "line" is visible, to indicate a positive test.

While being in the midst of a second and possibly facing an impending third wave of the H1N1v strain in the coming months, medical personnel are encouraged to contact their sales representative or technical support for utilization of the RIDT assays. A proposed webinar by the National Laboratory Training Network will also be available in the near future. By taking these steps, it is hoped that the RIDTs can become an effective tool to screen for influenza infection.

References

1. Centers for Disease Control and Prevention. Outbreak of swine-like origin influenza A (H1N1v) virus infection - Mexico, March-April 2009. *MMWR Morb Mortal Wkly Rep 2009;* **58**: 467-70.