

EVMS Journal Club  
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 Valerie Baur

P: In acutely ill patients presenting with “flu-like symptoms” during an H1N1 pandemic  
 I: does rapid antigen testing  
 C: compared to clinical impression alone  
 O: help guide physician decision making regarding diagnosis, treatment and disposition?

**\*\*FYI\*\***

Notes on Spectrum of Disease:

Increases in prevalence of a disease within a given population will not change **Sensitivity** or **Specificity** of a given test, as long as the spectrum of disease (i.e. the range of severity of an illness) remains constant.  
 However, the **Predictive Value** of a test *is affected* by the prevalence of the disease.

Article	Patient Group	Study Type	Outcome	Key Results	Weakness
<i>Rapid Antigen Tests for Diagnosis of Pandemic (Swine) Influenza A/H1N1.</i> Vasoo, R. et al. Clinical Infectious Diseases 2009; 49: 1090-1093	Convenience sample of 60 H1N1 positive specimens confirmed by RT-PCR. 24 specimens positive for other respiratory viruses served as control. 57% of pts initially presented to ED. 43% from PCP office.	Retrospective study Researchers blinded to RT-PCR results.	-BD Directigen: 46.7% sens, 100% spec -BinaxNOW: 38.3% sens, 100% spec -QuickVue: 53.3% sens, 100% spec Age and duration of symptoms did NOT correlate with positive results, however, higher viral loads did.	QuickVue significantly more sensitive (p<.01), but still low-moderate overall. Recommend RT-PCR on negative results.	Selection bias in study samples.  No standardized collection technique.  Samples refrigerated pending RT-PCR

<p><i>Ruling Out Novel H1N1 Influenza Virus Infection with Direct Fluorescent Antigen Testing.</i> Pollock, N. et al. Clinical Infectious Diseases 2009;49:e66-8</p>	<p>-112 Specimens from symptomatic health care workers or pts meeting CDC criteria for “ILI.” &gt;= 30 epithelials per well required for DFA. -3% of specimens were inadequate -Mean age 44.1yrs</p>	<p>-Prospective -Blinded -Compared DFA testing results to RT-PCR standard</p>	<p>-Relative to PCR: DFA Sens 93% (CI, 8%) DFA Spec 97% (CI, 4%) DFA NPV 96% (CI, 5%) DFA PPV 95% (CI, 7%)  -Only 3 false negatives with DFA “borderline inadequate samples”</p>	<p>-Highly sensitive and specific method of testing, comparable to PCR but less expensive and time intensive. -Subsequently increased specimen requirements to &gt;60 columnar epithelias</p>	<p>-Test still takes 1-4 hours. -Requires more technical expertise than rapid testing. -Neg results from inadequate samples not recorded, but positive ones were. -Only 2 pts &lt;18yrs, difficult to generalize. -NPV varies with disease prevalence.</p>
<p><i>Rapid-Test Sensitivity for Novel Swine-Origin Influenza A (H1N1) Virus in Humans.</i> Faix, D. et al. NEJM 2009; 361:7</p>	<p>-3066 specimens from border btwn CA and Mexico tested with RT-PCR -Compared to 767 matched Rapid test results.</p>	<p>Retrospective Single blinded</p>	<p>-Relative to PCR: -QuickVue test was 51% sensitive (95% CI , 35-67) Specificity 99% for swine flu -For seasonal flu, sens 63% (CI, 39-82)</p>	<p>-Rapid test sensitivity may vary according to Flu A subtype. -Test trends toward being less sensitive for swine flu than 2008 seasonal flu</p>	<p>-Overlapping CI for seasonal and swine-origin sensitivity of QuickVue test -Study performed at tail end of last flu season, needs more power. Only 18 cases of seasonal flu.</p>
<p><i>Analytical Sensitivity of Rapid Influenza Antigen Detection Tests for Swine-origin Influenza Virus (H1N1).</i> Chan KH, et al. Journal of Clinical Virology 2009; 45:205-207</p>	<p>Two isolates of S-OIV and one seasonal H1N1 visus (non-swine origin)</p>	<p>-Five different brands of rapid antigen tests tested for Sensitivity by serial dilution -QuickVue, Bianax, Directigen, Espline, and Wondfo rapid antigen tests -Compared to viral load by PCR</p>	<p>-Limit of detection for seasonal flu= TCID<sub>50</sub> 4.0 to 4.5 -Limit of detection for S-OIV= TCID<sub>50</sub> 3.9 to 4.7</p>	<p>Rapid antigen tests evaluated in this study have comparable sensitivity for detection of S-OIV and seasonal influenza viruses (no significant difference in limit of detection)</p>	<p>-Data does not reflect <b>clinical</b> sensitivity -Only 2 different virus isolates used.</p>

<p><i>Evaluation of Rapid Influenza Diagnostic Tests for Detection of Novel Influenza A (H1N1) Virus.</i> Balish A, et al. CDC MMWR 2009; 58:826-829</p>	<p>65 clinical respiratory specimens collected April-May 2009 -45 novel H1N1 pos -15 seasonal flu</p>	<p>CDC retrospectively evaluated multiple Rapid influenza diagnostic tests (RIDTs) on specimens already confirmed to have either seasonal or novel H1N1 flu. -BinaxNOW -Directigen -QuickVue</p>	<p>89-100% sens for H1N1 at High viral titers. Overall Sensitivity: BinaxNOW: 40% Directigen: 49% QuickVue: 69%</p>	<p>Overall sensitivity is low, especially at low virus titers. RIDTs appear to be more sensitive for seasonal flu.</p>	<p>Seasonal flu specimens were all present at higher viral titers, so cannot determine relative sensitivity of RIDTs.</p>
<p><i>H1N1 Early Detection Study.</i> Ginsburg, G. Duke Institute for Genome Sciences and Policy, DARPA (coming soon)</p>	<p>-Currently enrolling 500-800 undergrads with initial symptoms and their asymptomatic contacts.</p>	<p>Prospective Cohort study</p>	<p>???</p>	<p>Researchers hope to develop an RNA-based rapid test that can detect those infected with H1N1 earlier and with better sens/spec than current rapid antigen tests.</p>	<p>If successful, a pre-symptom test may take 2 years to be approved by FDA. Subject to selection bias</p>

Clinical Bottom Line:

Point of Care rapid antigen testing for H1N1 pandemic flu appears to have low to moderate sensitivity, which is comparable to the same test for seasonal flu outbreaks. Although positive test results can be managed with a high degree of certainty, negative test results must be interpreted within the context of current H1N1 prevalence and clinical suspicion. Since it is unrealistic to consider confirmatory testing for ED patients who are unlikely to be admitted, rapid antigen testing should be reserved for those patients who are considered to be at highest risk for complications (age <24y, pre-existing lung disease, immunocompromised states, etc.), and in whom test results will be used to guide medical decision making in patients likely to be admitted and at highest risk for complications.