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Evaluation of the 3M Rapid Detection Test for Respiratory Syncytial Virus (RSV) in Children during the Early Stages of the 2009 RSV Season▽

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We report the results of the 3M rapid detection respiratory syncytial virus (RSV) assay. This study includes pediatric patient results from nasopharyngeal swabs submitted from October to December 2009. There was a sensitivity of 74% and specificity approaching 100% compared to the PCR-based xTAG respiratory viral panel.

Respiratory syncytial virus (RSV) is the most common virus causing respiratory infections in young children and causes significant morbidity and mortality in this group (10, 12). The impact of RSV on children is well known, and the burden of outpatient and emergency department visits has now been well described: in children under 5 years old, it is associated with 20% of hospitalizations, 18% of emergency department visits, and 15% of office visits for acute respiratory infections from November through April (5). Each fall season, RSV infections are associated with a large increase in the volume of patients seen at our own pediatric emergency department, which is one of the busiest in the country, averaging about 61,000 visits per year and 5,500 admissions per year. An accurate rapid RSV test would allow clinicians, in this setting, to plan more appropriate management of respiratory illness in children.

Current testing for RSV includes serology, cell culture, direct immunofluorescent antibody tests (DFA), enzyme-linked immunoassays, and nucleic acid amplification (e.g., PCR) (6), but many of these modalities are not feasible in the emergency setting. Serology is not helpful in the diagnosis of an acute illness, cell culture requires precise collection and processing techniques, and DFA and PCR require specialized equipment and staff, which makes it difficult to provide timely results 24 h a day. Rapid antigen testing has become the most frequently used rapid test for RSV (http://www.cdc.gov/surveillance/nrevss/rsv/state.html).

During the 2008-2009 RSV season in New York, reported statewide prevalence was significant, but the clinical impression of physicians at our institution was that RSV disease was not being detected by the manual rapid CLIA (Clinical Laboratory Improvement Amendments)-waived test that we were using. When we compared our percent positives by rapid testing to New York state-wide NREVSS (National Respiratory and Enteric Virus Surveillance System) prevalence data from October 2008 through March 2009, we found that our percent positives were lower than those reported by other New York state hospitals. Clinical suspicion was further confirmed when a retrospective comparative analysis of rapid samples submitted from mid-November to mid-December 2008 demonstrated that the previously used manual test, QuickVue RSV (Quidel, San Diego, CA), had a sensitivity of <50% compared to that of the conventional viral culture test. In light of these findings and in preparation for the 2009-2010 RSV season, our laboratory switched to a new semiautomated 3M rapid detection test for RSV samples, which had been shown by preliminary reports to be more sensitive than other antigen-based RSV tests (2).

During the fall and winter (2009-2010), viral respiratory specimens were triaged in such a manner that, if requested by a clinician, a patient who was admitted to the inpatient unit would have both the 3M rapid detection RSV test and the xTAG respiratory viral panel (RVP) test. In this study, we determined the total number of patients between October and December 2009 who had the 3M rapid detection RSV test performed and then analyzed the subpopulation that had both tests performed, using the RVP as the gold standard. All specimens were nasopharyngeal (NP), obtained with flocked swabs, and placed in 3 ml of universal viral transport medium (BD). The 3M rapid detection RSV test (3M Medical Diagnostics, St. Paul, MN) was performed according to the manufacturer's recommendation and as previously described (7). The xTAG RVP assay (Luminex Molecular Diagnostics, Austin, TX) was performed on the same specimen as that used for the antigen test, with total nucleic acid (DNA plus RNA) extracted from 0.2 ml of nasopharyngeal specimens using the QIAamp MinElute virus spin kit (Qiagen, CA) and performed as previously described (9). The test comprised a multiplex reverse transcription-PCR (RT-PCR), exonuclease-phosphatase reaction, multiplex target-specific primer extension (TSPE), and bead hybridization. Finally, beads were sorted through a Luminex 200 IS system (Luminex Molecular Diagnostics, Inc.). The panel covered the following 12 viruses: influenza virus A, influenza virus A subtype H1, influenza virus A subtype H3, influenza virus B, respiratory syncytial virus subtype A, respiratory syncytial virus subtype B, parainfluenza 1 virus, parainfluenza 2 virus, parainfluenza 3 virus, human metapneumovirus, rhinovirus, and adenovirus. Clinical data for this study were obtained from the hospital and laboratory information

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TABLE 1. Comparison of both RSV A and B 3M rapid testing to the RVP, October to December 2009

Rapid antigen result	No. of isolates positive or negative for RSV A or B by the RVP	
	Positive	Negative
Positive	65	1
Negative	23	234

systems, transferred to a Microsoft Excel spreadsheet, and analyzed by SPSS using the two-tailed *t* or the chi-square tests. The Montefiore Medical Center internal review board approved this study.

Our 2009-2010 RSV season corresponded to what was seen nationally and reported by the CDC (http://www.cdc.gov/surveillance/nrevss/rsv/state.html). Between October and December 2009, rapid RSV tests were done on 2,067 samples from 1,846 pediatric patients with 470 positive results (23%). The percent positive at our hospital was significantly higher than the 13% positive from cumulative results reported by other institutions in New York state ($P < 0.05$, comparing October through December). This appeared to be a marked improvement over the previous RSV season but did raise some concerns over possible false-positive tests with the new 3M rapid test.

There were 328 samples from 303 distinct pediatric patients that had both the 3M rapid detection RSV test and RVP tests performed in 2009. Five specimens had indeterminate RVP results and were removed, allowing for the analysis of 323 comparison tests. The analysis of all the data is shown in Table 1. The RSV A and B rapid testing compared to the RVP had a sensitivity of 73.9% (confidence interval [CI], 64.7 to 83.0%), specificity approaching 100% (CI, 98.7 to 100%), positive predictive value of 98.5% (CI, 95.5 to 100%), and negative predictive value of 91.1% (87.6 to 94.5%). Analysis of the sensitivity and specificity for RSV A and RSV B individually showed that A had a slightly higher sensitivity (78%) than B (60%) with comparable specificity (99.6% for both) (Table 2).

When the 23 false negatives were compared to the 65 true positives, the results did not seem attributable to age (1.7 ± 0.46 years and 1.18 ± 0.32 years, respectively) or the presence of comorbidities (65.2% ± 19.5% and 60.0% ± 11.9%, respectively), which was similar in the two groups. There was a statistically significant difference in the percentage of patients who were started on oseltamivir in the false-negative rapid RSV group compared to that of the true-positive group (87.0% ± 13.8% versus 12.3% ± 8.0%, respectively), suggesting that antiviral prescribing practices may have been altered by the rapid testing results. In 16 of 20 patients in the false-negative group who were RSV positive on the RVP test, oseltamivir was discontinued in all but one patient, who additionally tested positive for influenza virus A. There was no difference in antibiotic administration (47.8% ± 20.4% versus 40% ± 11.9%, respectively) or length of stay (5.55 ± 3.97 days versus 6.08 ± 4.39 days, respectively) between the false-negative rapid RSV group and the true-positive group.

For the largest pediatric-serving emergency room in our system, 90% of rapid RSV tests were performed within 3 h (from collection to laboratory result) during this study period, compared with several days for the RVP. The lower-than-expected rapid test sensitivity and the long turnaround time of the RVP could affect clinical care (e.g., the unnecessary administration of antimicrobials, including oseltamivir, and possibly a failure to use appropriate hospital isolation practices). This reaffirms the need for a rapid test with high sensitivity and specificity in hospitals with high-volume emergency rooms (the test volume was more than 300 cases/month).

Although RSV antigen testing has become a widely used diagnostic test, the sensitivities of different tests vary. Here, we report successful use of the new 3M test compared to the QuickVue RSV test, but with a slightly lower sensitivity than previously reported when the 3M test was compared to the Luminex rather than the DFA. Ginocchio et al. found 86% sensitivity compared with DFA (3), but like them, we found that the 3M RSV has excellent specificity. Factors that affect antigen test sensitivity are not well understood but are probably multifactorial, including the stage of disease, the features at presentation, the type of specimen, and the gold standard for comparison.

Our study was the first direct comparison of the RVP to an RSV antigen test. We were able to show that there was no significant clinical or age difference between the true positives and false-negative specimens. One could conjecture that levels of viral shedding, which is known to persist for about 7 days and persists longer in significant lower respiratory tract disease, are lower than the detection level of the antigen tests (4). In our internal validation, the 3M test was shown to be more sensitive than two CLIA-waived tests, and a comparison to the New York state data shows that the 3M test is more sensitive than the other major antigen tests.

Specimen types can also influence the amount of virus in a specimen. Early studies showed that nasopharyngeal aspirates

TABLE 2. Comparison of the 3M RSV rapid test to the RVP, October to December 2009

Rapid antigen result	No. of isolates positive or negative by the RVP		% sensitivity (CI)	% specificity (CI)	Positive predictive value (%) (CI)	Negative predictive value (%) (CI)
	Positive	Negative				
RSV A			77.9 (68.1–87.8)	99.6 (98.7–100)	98.1 (94.6–100)	94.0 (91.0–96.9)
Positive	53	1				
Negative	15	234				
RSV B			60.0 (38.5–81.5)	99.6 (98.7–100)	92.3 (77.8–100)	96.7 (94.4–98.9)
Positive	12	1				
Negative	8	234				

were more likely to contain RSV than nasopharyngeal swabs (11). In our study, flocked NP swabs were used, which should improve the release of material into the viral transport medium. Most medical centers prefer to perform NP swabs. Two studies have shown that NP flocked swabs are equal or superior to NP aspirates (1, 8). Additionally all material was collected in 3 ml of viral transport medium. One manufacturer issued a suggestion that smaller volumes of viral transport may improve RSV antigen testing sensitivity, but no data are currently available supporting this claim (http://www.quidel.com/libraries/tb/RD/TB_rsv_sep2009.pdf).

The 3M test's excellent specificity may enable labs to redesign work flows. Analysis of our data indicates that only 2 of 88 (2%) patients who had RVP confirmation were coinfected with RSV and influenza virus. This may make it possible to triage specimens in a manner where RSV tests are run first and when positive further testing can be limited to only those patients who are hospitalized or severely ill. This would probably be cost-effective and medically reasonable. Finally, we are also considering the advisory concerning the volume of transport medium for nasopharyngeal specimens. Although it is logical that lower volumes might improve test sensitivity, further testing would be advisable before making this change.

In summary, the 3M rapid detection RSV test can be used with reliable specificity as a rapid test in the pediatric population during the RSV season. The rapid turnaround time makes it invaluable in the urgent care setting and for the management of patients during the initial part of their hospitalization. However, the sensitivity is lower than cited by prior comparisons to DFA or viral culture (2, 3), and if management strategies are to be employed based on the above sensitivity, negative results may have to be confirmed with PCR or another methodology. This is especially true for RSV B patients, though they will not be known on 3M rapid detection RSV testing alone.

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