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Performance of a Rapid Assay (Binax NOW) for Detection of Respiratory Syncytial Virus at a Children's Hospital over a 3-Year Period[▽]

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A rapid assay, Binax NOW RSV, was compared to viral culture for 14,756 pediatric respiratory specimens obtained from 2003 to 2006. There were 794 viral culture-confirmed respiratory syncytial virus infections. Sensitivity was 81%, and specificity was 93.2%. Sensitivity was greatest for neonates (91.1% versus 80.7% [$P < 0.01$]).

Respiratory syncytial virus (RSV) infection in children is associated with more than 90,000 hospital admissions/year nationally and as many as 1,000,000 deaths/year worldwide (12). It may be difficult to clinically differentiate RSV from other seasonal respiratory viruses. The rapid and accurate detection of RSV facilitates appropriate clinical management, including supportive care, hospital admission, isolation to decrease nosocomial transmission of the virus (3), antiviral treatment, and judicious antibiotic usage (1, 7, 10).

There are currently several commercially available methods for rapid RSV detection. Binax NOW RSV is an in vitro immunochromatographic assay for the detection of RSV fusion protein antigen. During the study period, this was the only rapid test used at our institution.

The study population consisted of all 14,756 consecutive fresh respiratory specimens collected from 10,341 patients at a 715-bed tertiary-care children's hospital between July 1, 2003 and June 30, 2006 for whom both rapid RSV test results and viral cultures were obtained. This study was exempt from the institutional review board. Specimens were obtained by respiratory therapists in a standardized manner and transported on ice to the virology laboratory. By institutional protocol, specimens tested by any rapid viral assay had concomitant viral tissue culture performed. Rapid assays were performed according to the manufacturer's package insert instructions. Results were interpreted by laboratory technicians based on the presence or absence of a pink-to-purple line, with appropriate positive and negative controls. Quality control measures included the use of internal kit positive and negative controls, as well as external laboratory controls on each test kit run.

All specimens were inoculated into three cell lines (rhesus monkey kidney, human foreskin fibroblast, and human lung carcinoma). This protocol allowed for detection of adenovirus, cytomegalovirus, herpes simplex virus, influenza viruses A and B, parainfluenza virus types 1 to 4, picornaviruses, and RSV.

Viral culture has classically been the reference standard for the diagnosis of RSV, and positive rapid assays associated with positive viral cultures were considered true positives. Emerging modalities such as PCR or immunofluorescence were not routinely utilized. Sensitivity, specificity, and likelihood ratios were calculated using standard 2-by-2 tables. Seasons were defined as extending from July 1 to June 30 of the given years. High-prevalence months accounted for >75% of positive RSV specimens for a particular season.

A total of 14,756 specimens were obtained from July 1, 2003 through June 30, 2006. Of these, 14,202 (96.2%) were nasal wash specimens, 287 (1.9%) tracheal aspirates, 118 (0.8%) nasopharyngeal swabs, 68 (0.5%) sputum specimens, and 59 (0.4%) bronchoalveolar lavage specimens. Viral cultures were negative for 11,289 (76.5%) specimens, while 3,467 (23.5%) specimens grew at least one virus. The most common viruses isolated were RSV (794 isolates), rhinoviruses (699), influenza A virus (694), parainfluenza viruses (358), adenovirus (307), cytomegalovirus (242), and influenza B virus (162). The median patient age was 13.5 months (range, 0 days to 28.7 years).

Patient age and specimen source were analyzed a priori. There were 643 true-positive, 13,015 true-negative, 947 false-positive, and 151 false-negative assay results during the study period. Performance is shown in Table 1. The ability to rapidly and accurately diagnose RSV in young infants is important for at least two reasons. First, the risk of complications such as apnea may lead to admission of a baby with RSV bronchiolitis who otherwise appears well. Second, the diagnostic evaluation of a febrile neonate may be altered by knowledge of RSV status, given the appreciable risk of urinary tract infections and the decreased rate of other serious bacterial infections in this patient population (8). The sensitivity of the test was consistently and significantly higher for neonates under the age of 1 month.

Performance was analyzed by specimen source, because many rapid assays, though licensed for upper respiratory tract specimens, are often used to test lower respiratory tract specimens, such as tracheal aspirates (4, 6). While decreased sensitivity was noted for non-nasal wash specimens relative to

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TABLE 1. Performance of the immunochromatographic assay compared to viral culture for the detection of RSV

Rapid assay group	Total no. of specimens	No. of RSV-positive cultures	% Sensitivity (CI)[a]	% Specificity (CI)	Likelihood ratio (CI) for positive RSV assay
Overall	14,756	794	81 (78–83.6)	93.2 (92.8–93.6)	11.9 (11.1–12.8)
2003–2004	5,131	164	70.1 (62.4–76.9)	94.2 (93.5–94.8)	12 (10.3–14)
2004–2005	4,606	237	84 (78.5–88.2)	90.6 (89.7–91.5)	9 (8.1–10)
2005–2006	5,019	393	83.7 (79.6–87.2)	94.6 (93.9–95.2)	15.6 (13.7–17.7)
High-prevalence mos	7,110	593	81.1 (77.7–84.1)	89.6 (88.8–90.3)	7.8 (7.2–8.4)
2003–2004	2,390	129	67.4 (58.6–75.3)	92.9 (91.7–93.9)	9.5 (7.8–11.5)
2004–2005	2,331	195	86.7 (80.9–90.9)	84.9 (83.2–86.4)	5.7 (5.1–6.4)
2005–2006	2,389	269	83.6 (78.6–87.7)	90.8 (89.5–92)	9.1 (7.9–10.5)
Low-prevalence mos	7,646	201	80.6 (74.3–85.7)	96.4 (95.9–96.8)	22.4 (19.5–25.6)
2003–2004	2,741	35	80 (62.5–90.0)	95.2 (94.3–96)	16.8 (13.1–21.3)
2004–2005	2,275	42	71.4 (55.2–83.8)	96.1 (95.2–96.9)	18.5 (14–24.6)
2005–2006	2,630	124	83.9 (75.9–89.6)	97.9 (97.2–98.4)	39.7 (30.1–52.3)
Age					
<30 days	951	56	91.1[b] (79.6–96.7)	88.5 (86.2–90.5)	7.9 (6.5–9.7)
≥30 days	13,805	738	80.7[b] (77.7–83.5)	93.5 (93.1–93.9)	12.5 (11.6–13.4)
Specimen type					
Nasal wash	14,202	778	81.2 (78.3–83.9)	93.1 (92.7–93.5)	11.8 (11–12.6)
Non-nasal wash	554	16	68.8 (41.5–87.9)	96.1 (94–97.5)	17.6 (10.3–30)

[a] CI, 95% confidence interval.
[b] $P = 0.01$.

nasal wash specimens, the preponderance of nasal wash specimens in this study population precluded statistical analysis.

Different studies have noted variable performance of similar assays. Five studies have evaluated Binax NOW with pediatric and adult populations (2, 6, 9, 11, 13); sensitivities of 74 to 100% were noted in pediatric studies using upper respiratory tract specimens, while the test demonstrated a sensitivity of only 33% for a small cohort of adult lower respiratory tract secretions. The specificities reported have been consistently higher, from 88.5 to 100%. In our center, the performance of this test, in terms of both sensitivity and specificity, was consistent over a 3-year period. The relatively lower sensitivity of the assay in the first year of the study may have been influenced by factors external to the test: the influenza A epidemic of 2003 resulted in an RSV epidemiologic curve that was both temporally shifted later into winter and of lower magnitude than that typically seen in this region. The stability of test performance in the latter two years of the study is reassuring, given the frequency with which clinical decisions are based on these rapid tests.

One limitation of the present study was that based on virology laboratory records, it was not possible to determine why patients had rapid viral testing performed. It is possible that, under certain circumstances, rapid assays are more clinically relevant than viral culture. For example, patients at the end of the natural course of RSV may have shedding of nonviable virions, which may be detected by a rapid assay but would not result in growth in tissue culture. Another limitation is that a sensitive method, such as direct fluorescence assays or RT-PCR, was not used to resolve discrepant results. Recent studies suggest that these methods may offer an advantage over traditional methods in some settings (5).

In summary, the Binax NOW RSV assay was sensitive and specific in detecting RSV infections over three consecutive winter seasons. This test performed particularly well for neonates, those children at highest risk for apnea and other severe complications of RSV disease. However, in view of the fact that both false-positive and false-negative results occurred, viral culture is recommended to confirm the rapid assay result and to detect the presence of other viruses for which rapid tests do not yet exist. The knowledge of the performance characteristics of different rapid viral assays is important for clinicians whose decisions may be influenced in part by the results of these diagnostic studies.

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