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Short Communication

Laboratory testing trends for respiratory syncytial virus, 2007–2011☆

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ABSTRACT

Background: Antigen detection tests have been the most common diagnostic assay used to detect and diagnose respiratory syncytial virus (RSV). The utility and increased sensitivity of polymerase chain reaction (PCR) tests have been reported; however, their use in US hospital laboratories is not well characterized.
Objective: To describe changes in RSV test types used by US hospital-affiliated laboratories, focusing on PCR testing prevalence.
Study design: Data were collected from 480 to 666 laboratories each RSV season (2007–2008 through 2010–2011) across 50 states, the District of Columbia, and Puerto Rico. A descriptive analysis was conducted using this convenience sample of RSV tests conducted from November to April each season. Total numbers and types of RSV tests performed were reported weekly and weekly proportions by test type were calculated. Kendall τ rank correlation was used to quantify associations between time and proportions of each test type.
Results: PCR tests accounted for 2%, 3%, 16%, and 21% of weekly tests (total range, 381,068–481,654 over 4 seasons) conducted each season from 2007 to 2011, respectively. The proportion of laboratories reporting $\geq$1 PCR tests was 4%, 5%, 10%, and 16%, respectively. Decreases in antigen testing and viral culture were similarly observed.
Conclusions: Although antigen detection was the predominant test type reported in the sample of US hospital laboratories for RSV testing, PCR use increased to >20% of tests reported. These results demonstrate the increasing contribution of PCR to RSV surveillance. RSV surveillance systems relying solely on antigen detection results will not capture an increasing proportion of RSV test results.

1. Background

Respiratory syncytial virus (RSV) circulates throughout the United States in the fall through spring with variable onset, peak month of activity, and season duration [1,2]. RSV surveillance data are reported from multiple sources, including the US Centers for Disease Control and Prevention (CDC), public health departments, and university-based medical centers. For RSV, the CDC collects and reports surveillance data regarding respiratory viruses through the National Respiratory and Enteric Virus Surveillance System (NREVSS), a national, laboratory-based passive surveillance system [3,4].

Testing for RSV can be performed using any of 3 types of laboratory diagnostic tests: (1) antigen detection; (2) polymerase chain reaction (PCR); and (3) culture (virus isolation [VI]). Antigen detection tests are the most common diagnostic assays used to detect RSV based on their low cost, ease of use, and rapid availability of results [5,6]. Published reports from the CDC NREVSS describing the RSV season (e.g., onset, offset, duration) are based only on antigen detection results, and recent reports indicate that 94–98% of

Abbreviations: CDC, US Centers for Disease Control and Prevention; DC, District of Columbia; NREVSS, National Respiratory and Enteric Virus Surveillance System; PCR, polymerase chain reaction; PR, Puerto Rico; RSV, respiratory syncytial virus; VI, virus isolation.

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Table 1
Characteristics of the RSVAlert® program (September 2007–August 2011).

Data collection period	Laboratories, *n*	States participating, *n*	Test types collected
9/8/2007 to 8/30/2008	626	50 (+DC)	Antigen, PCR, VI
9/6/2008 to 8/29/2009	666	50 (+DC)	Antigen, PCR, VI
9/5/2009 to 5/1/2010[a]	647/296[b]	50 (+DC)	Antigen, PCR, VI
8/14/2010 to 8/6/2011	480	50 (+DC, PR)	Antigen, PCR, VI

DC, District of Columbia; PCR, polymerase chain reaction; PR, Puerto Rico; RSV, respiratory syncytial virus; VI, virus isolation.
[a] Data were not collected from May 2010 to August 2010.
[b] Reduced laboratory site counts reflect program reduction beginning January 2010.

laboratories participating in this system use antigen detection as the primary method for diagnosis of RSV [4,7]. Recent studies have demonstrated the utility and increased sensitivity of PCR tests for the detection of respiratory viruses [8,9]. The frequency of PCR use to diagnose respiratory infections [10,11] in US hospital laboratories has not been well described.

2. Objectives

The objective of this analysis was to describe recent changes over time in the type of tests used for primary RSV detection by US hospital laboratories, with a focus on the use of PCR.

3. Study design

The RSVAlert® Program is a surveillance system designed to collect and characterize RSV test data in a near real-time reporting system at local, state, regional, and national levels [12].

Guiding recruitment characteristics for laboratories participating in RSVAlert® were: membership in the National Association of Children's Hospitals and Related Institutions, association with a large children's and/or metropolitan hospital that contains a neonatal and/or pediatric intensive care unit, high volume of RSV tests reported in prior years (≥10 tests per week during RSV peak season) [12], and good reporting compliance (i.e., at least 70%) in prior years. Geographic representation across states and local community areas was also considered during the annual recruiting process.

Data were collected from participating sites in all 50 states, the District of Columbia, and Puerto Rico (2010–2011 season only). Testing and laboratory methods used were based on individual institutional protocols and physician ordering practices. No attempt was made to standardize choice of patients tested or type of test performed by each reporting laboratory. Test data were reported within 14 days of the period stated; updates to weekly test data were accepted.

Participating laboratories reported weekly to provide data regarding the total number and results of diagnostic RSV tests by the type of test performed (i.e., antigen detection, PCR, or VI), and results of all tests performed [12]. Antigen-based detection included all methodologies used at the time of data collection, including immunochromatography and direct immunofluorescence; use was not stratified by test type. Absence of testing was also collected. Only primary test types and results were to be reported in cases where both primary and confirmatory tests were performed.

To describe clinical laboratory RSV testing trends, an analysis was conducted using a convenience sample of RSV test data. Analysis was limited to data reported during the months of November through April to provide a standard review period and enable subsequent comparisons with the CDC's seasonal data reporting. Data were aggregated weekly; each review period had a mean of 7 days.

To examine trends in the types of tests used, weekly proportions of each test type were calculated, averaged across the week in each review period, and reported as the mean weekly proportion of each test type. Kendall τ rank correlation was used to quantify associations between time (i.e., seasonal weeks from November 2007 through April 2011) and the proportion of each test type (i.e., weekly contribution of primary screening results from each test type from November 2007 through April 2011). The proportion of laboratories using PCR tests during each season of the review period was also analyzed. To control for sample bias, a secondary trend analysis was conducted using only the 220 laboratories that consistently participated during all 4 seasons.

4. Results

The number of laboratories participating each season ranged from 480 to 666 (Table 1). From January to May 2010, only 296 laboratories participated due to a program reduction. Antigen detection was the predominant test type reported during each of the 4 seasons (Table 2). The weekly proportion of RSV tests conducted using PCR increased significantly from November 2007 through April 2011, $\tau(101) = 0.77$, $P < 0.0001$. Conversely, the weekly proportions of RSV tests conducted through antigen detection and virus culture methods decreased during the same period, $\tau(101) = -0.60$, $P < 0.0001$, and $\tau(101) = -0.38$, $P < 0.0001$, respectively. The proportion of participating laboratories reporting ≥1 RSV test result using PCR increased from 4% in 2007–2008 to 16% in 2010–2011 (Table 2). The largest increases occurred between the 2008–2009 and 2010–2011 RSV seasons. During the review period, the proportion of laboratories using PCR tests also increased over time (Fig. 1A). Similar temporal trends were observed when data were analyzed for the subset of 220 consistently participating laboratories (Table 2, Fig. 1B).

5. Discussion

Although antigen detection remains the predominant test used for the detection of RSV in US hospital laboratories, the use of PCR has increased steadily over recent years. The proportion of tests conducted and the number of laboratories reporting ≥1 PCR tests increased each season. The largest increases were observed between 2009 and 2011.

A number of factors may have influenced the increased use of PCR tests for RSV detection. Multiplex PCR tests that include detection for RSV were first approved by the US Food and Drug Administration in January 2008 [13]. Additionally, the fact that the first available test for 2009 H1N1 influenza was a CDC-developed PCR test [14] may also have encouraged institutions to adopt PCR technology.

The results of this study are subject to several limitations. Laboratory recruitment for the RSVAlert® program is focused on children's hospitals and large metropolitan hospitals. This sampling method may overrepresent pediatric and/or urban populations as well as laboratories that routinely use PCR testing methods for RSV screening. These sites may differ from the total population because of their commitment to disease surveillance and/or their ability to commit resources to the reporting process. Also, a small proportion (1% in the 2010–2011 season) of RSVAlert® laboratories was unable to differentiate primary RSV tests from confirmatory tests due to