



Release Date: February 2007
Valid Until: April 2007

This educational activity is conducted as a part of the *Pediatric Respiratory Care Initiative*[™] (PRCI[®]), sponsored by Thomson Professional Postgraduate Services[®] (PPS), Secaucus, NJ.

Participants who wish to receive CME credit for this educational activity should do the following: (1) read the current issue; (2) complete the post-test and evaluation form. To apply for CME credit, return the completed post-test and evaluation form to:

Thomson Professional Postgraduate Services[®]
CME Dept. T314
150 Meadowlands Parkway
Secaucus, NJ 07094-2304

You may also fax the completed materials to 1 (201) 430-1441. If you have any questions, please call 1 (800) 606-6106 Ext. 8892.

Applicants will receive a certificate of participation from PPS by return mail within 6 to 8 weeks of the date of receipt of the completed evaluation form and post-test.

Learning Objectives

After studying the literature presented in this Pediatric Respiratory Care series, participants will be able to:

- Assess the utilization of commercial antigen detection assays during the influenza season in conjunction with use of nasopharyngeal samples for rapid diagnosing of influenza.
- Identify the challenges when diagnosing influenza due to the number of respiratory viruses circulating at any given time as well as the value of appropriate interpretation of test results for clinical decision making.
- Recognize that a confirmatory test like culture or RT-PCR is essential for confirmation of influenza during periods when the prevalence of influenza is low or has not been recognized in the community.

Target Audience

This educational activity is designed for pediatricians, primary care physicians, pediatric and family nurse practitioners, neonatologists, infectious disease specialists, allergists, pulmonologists, immunologists, and other healthcare professionals involved in the care and management of pediatric respiratory patients.

Thomson Professional Postgraduate Services[®] is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Thomson Professional Postgraduate Services[®] designates this educational activity for a maximum of 0.50 *AMA PRA Category 1 Credits*[™]. Physicians should only claim credit commensurate with the extent of their participation in the activity.

This CME activity is supported by an educational grant from MedImmune, Inc.

Clinical Insights, Pediatric Respiratory Care Initiative, and PRCI are trademarks used herein under license.

Off-Label Disclosure

Some of the drug treatments discussed in this issue may note uses not approved by the Food and Drug Administration. Articles containing such uses will be noted at the end of the article.

Copyright © 2007 Thomson Professional Postgraduate Services[®]. All rights reserved.

Clinical Insights[®] in

PEDIATRIC RESPIRATORY CARE

VOLUME 3, NUMBER 2 • FEBRUARY 2007

PEDRO A. PIEDRA, MD,* EDITOR-IN-CHIEF; JOHN DEVINCENZO, MD,[†] REVIEWER; KATHLEEN M. MAJOR,[‡] GRACE L. MCBRIDE,[§] SENIOR MANAGING EDITORS; MARK PALANGIO,^{||} SENIOR MEDICAL WRITER

Comparison of Rapid Influenza Diagnostic Tests: Challenges in Clinical Practice

Proper treatment of influenza depends on rapid diagnosis. However, clinical diagnosis of influenza is challenging because of concurrently circulating respiratory viruses. Laboratory techniques can aid in diagnosis and include direct antigen detection, virus isolation in cell culture, and detection of nucleic acid by polymerase chain reaction.

Several commercially available direct antigen detection assays for influenza yield results in 30 minutes.

Smit et al recently evaluated the new Binax NOW Influenza A & B combination assay, the Binax NOW Flu A assay, the Binax NOW Flu B assay, the Becton-

Dickinson Directigen Flu A+B assay, and immunofluorescence in comparison with viral culture for detecting influenza viruses. Respiratory samples were collected from 448 patients (mean age 34 years; range: 7 days to 101 years) who presented with influenza-like symptoms at Christchurch Hospital, New Zealand, during the 2004 winter influenza season.

A total of 521 samples were evaluated, including 338 nasopharyngeal swabs,

162 throat swabs, 19 nasal washes, and 2 swabs from unspecified sites. Influenza A virus was cultured from 113 samples and influenza B virus from 6 samples. Because of the small number of influenza B cases, the analysis was limited to influenza A.

There were no significant differences in the performance of the rapid antigen tests.

... sensitivities for all rapid antigen tests and immunofluorescence were significantly higher for nasopharyngeal samples than for throat swabs.

Sensitivities were 59% for Binax NOW Influenza A & B combination assay, 58% for the Binax NOW Flu A assay, and 53% Directigen Flu A & B assay for detecting influenza A virus compared with culture. In contrast, sensitivity with immunofluorescence compared with culture

was 80%. Antigen detection by immunofluorescence performed significantly better than Binax NOW Influenza A & B combination assay ($P < 0.0001$), Binax NOW Flu A assay ($P < 0.0001$), and Directigen Flu A+B assay ($P = 0.0001$). Furthermore, sensitivities for all rapid antigen tests and immunofluorescence were significantly higher for nasopharyngeal samples than for throat swabs. Specificity for each of the 3 rapid antigen tests was $\geq 99\%$, and the specificity for immunofluorescence was 98%.

Continued

Disclosures:

- * Dr Piedra is professor of molecular virology and microbiology, and pediatrics at Baylor College of Medicine. He has indicated relevant financial relationships as noted: he receives grant/research support from MedImmune, Inc.; is a speaker for MedImmune, Inc.; is an expert witness for Sanofi-Pasteur; and is an ad hoc consultant for GlaxoSmithKline, MedImmune, Inc., and Sanofi-Pasteur.
- † Dr DeVincenzo is an Associate professor of pediatrics and molecular sciences at the University of Tennessee. He has indicated relevant financial relationships as noted: he receives grant/research support from Alnylam Pharmaceuticals Inc., is a retained consultant for Tibbotec Inc.; he receives grant/research support and is a retained consultant for Arrow Pharmaceuticals Inc.; Becton Dickinson Inc., and MedImmune Inc.
- ‡ Ms Major is a senior managing editor for Thomson Professional Postgraduate Services[®]. She has indicated no relevant financial relationships.
- § Ms McBride is a senior managing editor for Thomson Professional Postgraduate Services[®]. She has indicated no relevant financial relationships.
- || Mr Palangio is a senior medical writer for Thomson Professional Postgraduate Services[®]. He has indicated no relevant financial relationships.



Comparison of Rapid Influenza Diagnostic Tests *(Continued)*

These results indicate that commercial antigen detection assays are valuable tools for the rapid diagnosis of influenza and that the 3 rapid tests perform similarly for the detection of influenza A. The use of nasopharyngeal samples over throat swabs for all rapid detection methods is encouraged. The major limitation of antigen detection assays is the suboptimal sensitivity. Consequently, confirmatory testing is strongly recommended.

Immunofluorescence is the preferred rapid diagnostic test for laboratories with access to this method.

Smit M, Beynon KA, Murdoch DR, Jennings LC. Comparison of the NOW Influenza A & B, NOW Flu A, NOW Flu B, and Directigen Flu A+B assays, and immunofluorescence with viral culture for the detection of influenza A and B viruses. *Diagn Microbiol Infect Dis.* 2007;57:67-70.

COMMENTARY

JOHN DEVINCENZO, MD, is Associate Professor of Pediatrics and Molecular Sciences, University of Tennessee, Memphis, Tennessee.

Diagnosing influenza in a specific patient has many purposes and, for each purpose, the different influenza diagnostic tests have advantages and disadvantages. One of the aims is to institute a specific antiviral treatment for patients and a postexposure antiviral prophylaxis for their contacts. Another reason to establish a diagnosis may be to avoid the need for alternative diagnostic and therapeutic maneuvers. A third might be to investigate the local influenza epidemic and to institute the appropriate hospital infection control practices for patients. To initiate antiviral therapy, a clinical diagnosis of influenza during a recognized local epidemic may be sufficient. If a specific viral lab diagnosis is needed, then rapidity is prudent because the efficacy of therapy depends on prompt administration of the antiviral. In this case, the rapid antigen tests may be preferred, even with their relative lack of sensitivity (as described by Smit et al). DFA testing, although more sensitive, cannot generate results while the patient waits. Regardless of which test is used, specimen quality is paramount. Smit et al evaluated nasal swabs, but did not mention the quality of these specimens. The greater the quantity of respiratory epithelial cells obtained in the specimen, the more sensitive the test result. These diagnostic difficulties underscore the preference for influenza prevention, when possible, over therapy because an accurate individual patient diagnosis is not indicated for the application of the influenza vaccine.

During the peak of influenza epidemics, a positive test result is highly likely to correspond with true influenza illness, whereas a negative test result indicates a low likelihood of influenza illness.

Interpretation of Rapid Influenza Tests in Children: Critical to Clinical Decision Making

Accurately and quickly identifying influenza illness in children helps in clinical decision making and improves outcomes. Despite the availability of a variety of rapid diagnostic tests, practice guidelines on the use of these tests are limited. Furthermore, interpretation of test results is complicated by test characteristics and influenza prevalence.

In a recent study, Grijalva and colleagues sought to determine the times at which rapid tests are most predictive of influenza infection. The New Vaccine Surveillance Network (NVSN) prospectively enrolled children <5 years of age who were hospitalized with respiratory symptoms or fever from October 2000 through September 2004, in Davidson County, Tennessee; Monroe County, New York; and Hamilton County, Ohio

(Hamilton County began participation in 2003). On enrollment, nasal and throat swabs were obtained and tested for influenza virus by viral culture and reverse-transcription polymerase chain reaction (RT-PCR). Sensitivity and specificity of provider-ordered rapid influenza tests were determined by comparing results with those of viral culture and RT-PCR. Additionally, NVSN outpatient surveillance was performed during the 2002-03 and 2003-04 influenza seasons, and trends in weekly predictive values of the rapid tests were estimated over those influenza seasons.

During the 4 consecutive years of surveillance, 2,797 hospitalized children with respiratory symptoms or fever were enrolled and tested for influenza by viral culture and RT-PCR, among whom 160 (6%) had confirmed

Continued



Interpretation of Rapid Influenza Tests in Children *(Continued)*

influenza infection. A total of 270 children (10%) had a rapid influenza test. Rapid influenza tests had an overall sensitivity of 63% (95% confidence interval [CI], 47%-78%) and specificity of 97% (95% CI, 94%-99%).

During the mild 2002-03 influenza season, the prevalence of influenza in symptomatic outpatient children peaked at 21% and stayed above 10% for approximately 4 weeks. During the moderately severe 2003-04 influenza season, influenza prevalence peaked at 60% and remained above 20% for approximately 6 weeks. The positive predictive value of the rapid tests was $\geq 80\%$ when influenza prevalence was $\geq 15\%$, but decreased to $< 70\%$ when influenza prevalence was $< 10\%$. At the beginning of the 2002-03 season when the prevalence of influenza in a febrile respiratory illness was 5%, the predicted value of a

positive test was 50%. In this setting a positive test was equally likely to represent a true infection or a false positive result.

This study showed that Influenza prevalence varies between and within seasons, and that rapid tests are of limited use when the prevalence is $< 10\%$. During the peak of influenza epidemics, a positive test result is highly likely to correspond with true influenza illness, whereas a negative test result indicates a low likelihood of influenza illness. The study investigators concluded that appropriate interpretation of rapid influenza tests requires local influenza surveillance and timely communication of this information to the practitioners.

Grijalva CG, Poehling KA, Edwards KM, et al. Accuracy and interpretation of rapid influenza tests in children. *Pediatrics*. 2007;119:e6-e11.

Clinical Insights® in Pediatric Respiratory Care Post-Test

1. Which of the following statements is false regarding the results of the Smit et al study?
 - a. The 3 commercial antigen detection assays were similarly effective.
 - b. Sensitivities for all rapid antigen tests were significantly higher for nasopharyngeal samples than for throat swabs.
 - c. The major limitation of antigen detection assays is the suboptimal specificity.
 - d. Immunofluorescence is the preferred rapid diagnostic test.
2. Which of the following statements is false regarding the results of the Grijalva et al study?
 - a. Rapid tests are of limited use when the influenza prevalence is $< 10\%$.
 - b. Rapid tests are of limited use when the influenza prevalence is $\geq 15\%$.
 - c. A positive test result during the peak of influenza epidemics probably corresponds with true influenza illness.
 - d. A negative test result during the peak of influenza epidemics indicates a low likelihood of influenza illness.

1. c. The major limitation of antigen detection assays is the suboptimal specificity.
 2. b. Rapid tests are of limited use when the influenza prevalence is $< 10\%$, not $\geq 15\%$.

PRCI MISSION STATEMENT

The PRCI is a multicomponent educational program on pediatric respiratory disorders designed for pediatricians, primary care physicians, pediatric and family nurse practitioners, neonatologists, infectious disease specialists, allergists, pulmonologists, immunologists, and other healthcare professionals involved in the care and management of pediatric respiratory patients. PRCI programs address issues concerning asthma, respiratory syncytial virus, and other respiratory tract infections and disorders. Methods to prevent, control, and treat respiratory illnesses in children are also evaluated.

For more information about upcoming PRCI® CME activities, visit us at www.ppscme.org.

You are receiving this email because you are a member of the Thomson Healthcare Community. If you would like to be removed from all future PRCI Clinical Insights® in Pediatric Respiratory Care e-blasts, please send a blank e-mail to: leave-542645-39890312A@info.tshis.com.

