

Impact of Rapid Diagnosis on Management of Adults Hospitalized With Influenza

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Background: Rapid influenza testing decreases antibiotic and ancillary test use in febrile children, yet its effect on the care of hospitalized adults is unexplored. We compared the clinical management of patients with influenza whose rapid antigen test result was positive (Ag+) with the management of those whose rapid antigen test result was negative or the test was not performed (Ag0).

Methods: Medical record review was performed on patients with influenza hospitalized during 4 winters (1999-2003). Hospital policy mandated influenza testing (antigen or culture) for all patients with acute cardiopulmonary diseases admitted from November 15 through April 15. A subset of patients participated in an epidemiological study and had reverse-transcriptase polymerase chain reaction or serologic testing performed. Clinical data from Ag+ and Ag0 patients were compared.

Results: Of 166 patients with available records, 86 were Ag+ and 80 were Ag0. Antibiotic use (74 [86%] of 86 patients vs 79 [99%] of 80 patients; $P = .002$) was less and antibiotic discontinuance (12 [14%] of 86 patients vs 2

[2%] of 80 patients; $P = .01$) was greater in Ag+ compared with Ag0 patients. No significant differences in antibiotic days, length of hospital stay, or antibiotic complications were noted. Antiviral use (63 [73%] of 86 patients vs 6 [8%] of 80 patients; $P < .001$) was greater in Ag+ than Ag0 patients. Antigen status was independently associated with withholding or discontinuing antibiotics in multivariate analysis. Of 44 Ag+ patients deemed low risk for bacterial infection, 27 continued to receive antibiotics despite positive influenza test results. These patients more commonly had pulmonary disease and had significantly more abnormal lung examination results ($P = .005$) compared with those in whom antibiotics were withheld or discontinued.

Conclusions: Rapid influenza testing leads to reductions in antibiotic use in hospitalized adults. Better tools to rule out concomitant bacterial infection are needed to optimize the impact of viral testing.

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ADVANCES IN DIAGNOSTIC technology allow the rapid identification of a number of common viral infections.¹⁻⁴ Rapid tests for influenza and respiratory syncytial virus using enzyme immunoassay methods are commercially available and widely used.⁵⁻⁷ In addition, diagnostic testing using molecular technology continues to evolve in terms of improved sensitivity and number of detectable pathogens.^{8,9} The rapid diagnosis of influenza in hospital settings is important for infection control and potential antiviral therapy. However, most common respiratory viruses require only standard infection control practices and antiviral therapies are not yet available. Yet, it is possible that timely diagnoses of such viruses may still result in benefits for patient care. When used in febrile children, rapid tests for influenza viruses, respira-

tory syncytial virus, and enterovirus have been shown to reduce antibiotic use, ancillary diagnostic testing, and length of hospital stays.¹⁰⁻¹⁴ Because essentially no data are available for adults, we retrospectively compared the clinical management of adults hospitalized with documented influenza in whom rapid influenza test results were positive on admission with those in whom the diagnosis of influenza was made by other means and, thus, the diagnosis was either delayed or unavailable during the hospital course.

METHODS

PATIENTS

Retrospective medical record reviews were performed on patients older than 18 years who had documented influenza A or B and were hospitalized at Rochester General Hospital during 4

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winters (1999-2003). During this period, hospital infection control policy mandated influenza testing between November 15 and April 15 for all patients with acute cardiopulmonary symptoms with the exception of acute coronary syndrome, pulmonary embolism, or witnessed aspiration. Combined nasal and pharyngeal swab results were obtained on admission, and viral culture was performed on all samples until influenza activity in the hospital was confirmed. Once influenza activity was documented, rapid testing of all samples was instituted, followed by viral culture if antigen test results were negative. Positive rapid test results were communicated immediately by the laboratory technician to the patient's nurse by telephone, and patients were placed on droplet isolation. A subset of patients agreed to participate in an epidemiological study of respiratory illnesses and had reverse-transcriptase polymerase chain reaction (RT-PCR) and serologic tests performed in addition to antigen testing and viral culture. The RT-PCR and serologic testing was batched and performed several months after hospital discharge.

DATA COLLECTION

Demographic data, medical history, medication use, and physical findings on admission were collected by review of the emergency department and admission notes by study personnel (A.R.F. and Y.M.), and data were recorded on standardized forms. Laboratory data collected included admission white blood cell count, blood and sputum bacterial culture results, and chest radiograph (CXR) readings within 72 hours of admission. In those patients in whom multiple CXRs were obtained in the 72-hour period, all abnormal readings were recorded. Hospital length of stay, intensive care use, days of antibiotics in the hospital, discharge medications, and deaths were also recorded. The primary investigator (A.R.F.) reviewed medical records to determine if influenza or viral infection was included in the differential diagnosis of the admitting health care providers (physicians, nurse practitioners, or physician assistants), as evidenced by a statement in a written note or an order for influenza testing. Records were examined for evidence that the influenza test result was known and to determine if a specific change in management was undertaken in response to that information (ie, add antiviral agent, discontinue or change antibiotic agent, or hospital discharge). Medical records were further reviewed for complications possibly related to antibiotics (diarrhea, drug rash, fungal infection, or renal, hepatic, or bone marrow dysfunction). The study was approved by the University of Rochester research subjects review board and the Rochester General Hospital clinical investigation committee.

LABORATORY ANALYSIS

Rapid Antigen and Viral Culture

Commercially available kits (Directigen kits; Becton Dickinson, Franklin Lakes, NJ) were used according to the manufacturer's specifications to detect the presence of influenza A proteins.

Nasal and pharyngeal swab samples were inoculated onto rhesus monkey kidney cells, and virus growth was confirmed by indirect immunofluorescence using influenza A and B-specific monoclonal antibodies (Bartels-Trinity Biotech Co, Carlsbad, Calif).

RT-PCR and Serologic Testing

Reverse-transcriptase-PCR for influenza was performed on 250- μ L of nasal and pharyngeal swab samples using single-tube nested reactions with primers from the conserved region of the influenza A matrix genes.

Enzyme immunoassay was used to measure serum IgG titers to influenza using lysates from representative isolates of circulating influenza A and B strains.¹⁵ A 4-fold or greater increase in titer between acute and convalescent serum samples at least 1 month after vaccination was considered diagnostic of infection.

DATA ANALYSIS

Patients with influenza were grouped into 2 categories: patients with a positive rapid antigen test result (Ag+) and those whose rapid antigen test results were negative or in whom the test was not performed (Ag0). Comparison of demographics, clinical variables, and management of these 2 groups was undertaken. A multivariate analysis was performed to determine which factors were independently associated with a decision to withhold or discontinue antibiotic therapy. In addition, a secondary analysis was performed, which eliminated patients deemed at high risk for bacterial infections (symptoms ≥ 7 days before admission, intensive care required, white blood cell count $\geq 12 \times 10^3/\mu$ L or $\geq 10\%$ band forms, infiltrate on CXR, and positive blood culture or positive adequate sputum culture result).

STATISTICAL ANALYSIS

χ^2 and Fisher exact tests were used to compare proportions. Parametric testing (*t* test) and nonparametric testing (Kruskal-Wallis test) were used to compare means as appropriate. For multivariate analysis, logistic regression was used to calculate odds ratios with 95% confidence intervals using JMP, version 5.1.2, and SAS statistical software (SAS Institute Inc, Cary, NC).

PHYSICIAN SURVEY

A 4-question survey regarding antibiotic use in influenza-infected patients was mailed to 150 internists or family practice physicians on the medical staff of Rochester General Hospital. A brief case of a 70-year-old woman with cough and fever who was started on antibiotics at admission was described. Physicians were asked if the official CXR report was "no acute disease" and the rapid influenza test result was positive, what reasons would prompt them to continue antibiotic therapy (**Figure**).

RESULTS

Of 166 patients with influenza, 86 were Ag+ and 80 were Ag0. Of these patients, 105 (63%) participated in the epidemiological research study. Most infections (95%) were influenza A, including all the rapid antigen-positive results, with few influenza B infections (5%) identified by culture or serologic test result. Of the 80 Ag0 patients, 61 had testing performed, with negative results, and 19 did not have antigen testing done. The methods of diagnosis for the Ag0 group included culture-positive results for 30 patients, culture-negative results and RT-PCR-positive results for 30 patients, and seropositive-only results for 20 patients. Influenza testing was ordered by the emergency department or admitting health care provider for 78 (47%) of the 166 patients. Of the 88 patients who would have been missed if the influenza screening program were not in place, 37 (42%) were potentially infectious at admission (ie, culture or antigen

A 70-year-old woman comes to the ED with a cough and high fever. She is sick but not critically ill. The preliminary reading from the ED of the CXR is atelectasis vs pneumonia. After blood cultures, she begins receiving ceftriaxone and azithromycin. After antibiotics are administered, the rapid test result for influenza A comes back positive.

1. If the official CXR reading is "no acute disease," which of the following would lead you to continue antibiotic therapy in this patient? Check all that apply:
 - a. The patient is on a pathway for community-acquired pneumonia and improving.
 - b. I do not trust the CXR report.
 - c. I do not trust the flu test.
 - d. IV medications are needed to justify continued hospitalization.
 - e. I am worried about concomitant bacterial infection.
 - f. Other _____
2. If you answered more than 1 reason for continuing antibiotic therapy in question 1, please enter the letter of the most important reason: _____
3. Which of the following allow you to feel comfortable discontinuing antibiotic therapy in this patient?
 - a. A constellation of currently available tests (ie, negative blood and sputum culture results, normal WBC count, and negative CXR result).
 - b. All of the above with new validated tests to assess risk of bacterial infections (ie, ESR, CRP level, and procalcitonin level).
 - c. Practice guidelines from a professional association (ie, ACP or IDSA).
 - d. Other _____
4. What risk of bacterial disease would you accept and still discontinue the antibiotic therapy?
 - a. 0%
 - b. $\leq 5\%$
 - c. $\leq 10\%$
 - d. $\leq 20\%$

Figure. Survey asking physicians if the official chest radiograph (CXR) result was "no acute disease" and the rapid influenza test result was positive, what reasons would prompt them to continue antibiotic therapy. ACP indicates American College of Physicians; CRP, C-reactive protein; ED, emergency department; ESR, erythrocyte sedimentation rate; IDSA, Infectious Diseases Society of America; IV, intravenous; and WBC, white blood cell.

positive). Antibiotic use was high in the entire group (92%), although testing for bacterial infection was not universal, with only 115 (69%) and 66 (40%) of 166 patients having blood and sputum cultures done, respectively. Of the 153 antibiotic recipients, 93 (61%) received combination therapy, which most commonly consisted of ceftriaxone and a macrolide (78 [84%] of the 93 patients). The remaining 60 patients (39%) received monotherapy: macrolide (n=20), quinolone (n=23), β -lactam (n=16), and other (n=1).

The demographic characteristics (age, race, and sex) of the 2 groups were similar; however, significant differences were noted in the frequency of certain underlying conditions (**Table 1**). Among Ag0 patients, the rates of underlying chronic obstructive pulmonary disease, inhaled corticosteroids, and home oxygen use were significantly greater than among Ag+ patients. In contrast, cardiac disease was more common in Ag+ patients. Although the influenza vaccination rate was higher in the Ag+ group, vaccination status was not recorded in half of this group. The clinical presentation of the Ag+ patients was also somewhat different compared with the Ag0 group (**Table 2**). Patients who were Ag+ had a shorter duration of illness before presentation to the hospital, were more often febrile, and were less likely to experience wheezing on examination than were Ag0 patients. Despite these differences, there were no significant differences in peripheral white blood cell count, infiltrates noted on CXRs, or positive bacterial culture results.

Table 1. Patient Characteristics

Characteristic	Ag0 Patients (n = 80)*	Ag+ Patients (n = 86)*	P Value
Age, y†	74 \pm 13	75 \pm 16	.66
Female sex	45 (56)	41 (48)	.28
White race	72 (90)	76 (88)	.80
Cardiac disease	35 (44)	52 (60)	.03
Pulmonary disease	52 (65)	30 (35)	<.001
COPD	43 (54)	26 (30)	.003
Diabetes mellitus	17 (21)	23 (27)	.47
No. of medical diagnoses†	3.3 \pm 1.6	3.6 \pm 2.0	.29
Inhaled corticosteroids used	25 (31)	14 (16)	.03
Home oxygen use	18 (22)	6 (7)	.007
Influenza vaccination‡	52 (74)	35 (85)	.02

Abbreviations: Ag0, rapid antigen test result was negative or the test was not performed; Ag+, rapid antigen test result was positive; COPD, chronic obstructive pulmonary disease.

*Data are given as number (percentage) of each group unless otherwise indicated.

†Data are given as mean \pm SD.

‡Vaccination status was not available for all patients. For the Ag0 group, n=70; and for the Ag+ group, n=41.

Table 2. Illness Characteristics

Characteristic	Ag0 Patients (n = 80)*	Ag+ Patients (n = 86)*	P Value
Length of symptoms, d†	4.6 \pm 3.0	3.3 \pm 3.4	<.001
WBC count, $\times 10^3/\mu\text{L}$ ††	10.9 \pm 5.1	9.7 \pm 5.2	.14
Temperature $\geq 37.5^\circ\text{C}$	46 (58)	69 (80)	.002
Respiratory rate/min†	27 \pm 8	25 \pm 6	.07
Heart rate, beats/min†	106 \pm 23	100 \pm 22	.09
Oxygen saturation, %†	87 \pm 8	90 \pm 8	.02
Wheezes	51 (64)	41 (48)	.04
Rales	44 (55)	34 (40)	.06
Rhonchi	48 (60)	48 (56)	.64
CXR infiltrates	19 (24)	17 (20)	.58
Intensive care	17 (21)	12 (14)	.23
Death	6 (8)	4 (5)	.52
Positive blood culture result	1 (1)	1 (1)	>.99
Positive adequate sputum culture result	8 (10)	6 (7)	>.99

Abbreviations: Ag0, rapid antigen test result was negative or the test was not performed; Ag+, rapid antigen test result was positive; CXR, chest radiograph; WBC, white blood cell.

*Data are given as number (percentage) of each group unless otherwise indicated.

†Data are given as mean \pm SD.

††One patient with chronic lymphocytic leukemia and a WBC count of $72 \times 10^3/\mu\text{L}$ was excluded.

Documentation in the medical record that the health care provider was aware of the influenza test result was noted in 83 (97%) of 86 Ag+ patients in contrast to 8 (10%) of 80 patients with negative test results. In 27 (32%) of 86 Ag+ patients, a change in management in response to the result could be discerned. In 12 (14%) of 86 patients, all antibiotics were discontinued; 4 (5%) had 1 of 2 antibiotics discontinued; and in 11 (13%) patients, intravenous antibiotics were changed to oral antibiotics. No mention of early discharge because of a viral diagnosis could be found in any of the medical

Table 3. Comparison of Medical Management in Ag0 and Ag+ Patients

Variable	Ag0 Patients (n = 80)*	Ag+ Patients (n = 86)*	P Value
Antibiotic used	79 (99)	74 (86)	.002
Length of antibiotic use, d†‡	6.9 ± 3.2	6.2 ± 5.0	.29
Combination antibiotics used	47 (59)	46 (53)	.53
Single antibiotic used	32 (40)	28 (33)	.33
Antibiotics discontinued because of influenza diagnosis	2 (2)	12 (14)	.004
Discharged from the hospital while taking antibiotics	51 (64)	38 (44)	.006
Antiviral agent used	6 (8)	63 (73)	<.001
Length of hospital stay, d†	7.9 ± 4.2	9.6 ± 10.0	.16
Complications§	7 (9)	8 (9)	>.99
Diarrhea	3 (4)	2 (2)	.67
<i>Clostridium difficile</i> colitis	1 (1)	2 (2)	>.99
Thrush	2 (2)	1 (1)	.60
Rash	2 (2)	2 (2)	>.99
Abdominal pain	1 (1)	0	.48
Pancytopenia	0	1 (1)	>.99

Abbreviations: See Table 2.

*Data are given as number (percentage) of each group unless otherwise indicated.

†Data are given as mean ± SD.

‡Calculated only using inpatient days.

§Some patients had more than 1 complication. Individual percentages may not total the overall percentage for complications.

records, and length of hospital stay was similar in the 2 groups. Significant differences between the Ag+ and Ag0 patients were noted in the antimicrobial management of patients, as outlined in **Table 3**. The number of patients who had antibiotics prescribed in the hospital or were discharged home with oral antibiotics was significantly less in the Ag+ group, although the mean number of antibiotic days and rates of combination therapy were not significantly different. In addition, no difference in rates of antibiotic-related complications between groups was found.

As expected, the use of antiviral medications was significantly greater in Ag+ compared with Ag0 patients. Of interest, 24 (39%) of the 62 patients treated had symptoms for longer than 48 hours. (One patient did not have length of symptoms recorded.) There were no significant differences in outcomes (intensive care use, length of stay, or death) in those receiving antiviral agents within the recommended 48-hour window compared with those treated outside the recommended window and those who did not receive antiviral therapy.

Because differences in clinical presentation of the Ag+ and Ag0 groups could confound assessment of the impact of rapid test results on clinical management, a multivariate analysis was performed using multiple variables (**Table 4**). A positive rapid test result was independently associated with a decision to withhold or discontinue antibiotic therapy, with an odds ratio of 6.90 ($P = .005$). Although the presence of abnormal findings on lung examination and infiltrates on CXR were associated with continuing antibiotic therapy, these factors did not reach statistical significance.

Table 4. Multivariate Analysis: Clinical Features of Patients in Whom Antibiotics Were Withheld or Discontinued Compared With Those in Whom Antibiotics Were Continued

Variable	Odds Ratio (95% Confidence Interval)	P Value
Underlying cardiac disease	2.00 (0.70-5.80)	.19
Underlying COPD	0.71 (0.20-2.00)	.53
Symptoms >3 d	0.73 (0.20-2.10)	.58
Temperature ≥37.5°C	0.83 (0.30-2.70)	.75
Any abnormality on lung examination	0.32 (0.10-1.00)	.06
WBC count >12 × 10 ³ /μL	0.95 (0.20-3.30)	.94
CXR with infiltrate	0.22 (0.09-1.50)	.22
Positive rapid flu test result	6.90 (2.00-32.70)	.005

Abbreviations: COPD, chronic obstructive pulmonary disease; CXR, chest radiograph; WBC, white blood cell.

Table 5. Comparison of Ag+ and Ag0 Patients With Clinical Features Deemed at Low Risk for Bacterial Infections

Variable	Ag0 Patients (n = 26)*	Ag+ Patients (n = 44)*	P Value
Antibiotic used	25 (96)	32 (73)	.02
Antibiotics discontinued because of influenza diagnosis	0	5 (11)	.06
Length of antibiotic use, d†‡	6.9 ± 3.8	5.3 ± 3.8	.09
Discharged with antibiotics	15 (58)	16 (36)	.13
Antiviral agent used	0	31 (70)	<.001
Length of hospital stay, d†	7.9 ± 4.9	7.4 ± 1.2	.52
Complications	2 (8)	1 (2)	.55

Abbreviations: See Table 2.

*Data are given as number (percentage) of each group unless otherwise indicated.

†Data are given as mean ± SD.

‡Calculated only using inpatient days.

A total of 44 Ag+ and 26 Ag0 patients were considered at low risk for bacterial infections (as described in the "Data Analysis" subsection of the "Methods" section), and were included in a secondary analysis. As found for the entire group, there was significantly greater antiviral and less antibiotic use in the Ag+ vs Ag0 patients (**Table 5**). In addition, a trend toward fewer in-hospital antibiotic days was observed among those with a positive rapid test result. To assess whether differences in patient characteristics or presentation of these 44 Ag+ "low bacterial risk" patients might have affected antibiotic use, clinical variables for the 17 patients in whom antibiotics were not used or were curtailed were compared with those of the 27 individuals in whom antibiotics were continued (**Table 6**). The group that continued to receive antibiotics showed a trend toward older age, more underlying lung disease, and lower oxygen saturation on admission compared with those who received no antibiotics. In addition, abnormalities on lung examination were significantly more common in the group that continued to receive antibiotics. Despite no difference in the rate of radiographic abnormalities, the anti-

Table 6. "Low-Risk" Ag+ Patients in Whom Antibiotics Were Either Not Used or Discontinued vs Ag+ Patients in Whom Antibiotics Were Continued

Variable	No Antibiotics or Antibiotics Discontinued (n = 17)*	Antibiotics Continued (n = 27)*	P Value
Age, y†	66 ± 23	72 ± 13	.27
Home (independent)	11 (65)	14 (52)	.54
Lung disease	3 (18)	11 (41)	.18
COPD	2 (12)	9 (33)	.16
Cardiac disease	11 (65)	20 (74)	.52
Smokers	6 (35)	19 (70)	.03
Bronchodilator used	1 (6)	11 (41)	.01
Wheezing	3 (18)	15 (56)	.03
Rales	2 (12)	9 (33)	.16
Rhonchi	5 (29)	17 (63)	.07
Any abnormal lung finding	8 (47)	24 (89)	.005
Oxygen saturation, %†	94 ± 4	90 ± 8	.06
CXR result			
No acute disease	12 (71)	18 (67)	>.99
Atelectasis vs pneumonia	2 (12)	4 (15)	>.99
Admission diagnosis of pneumonia	1 (6)	9 (33)	.06

Abbreviations: Ag+, rapid antigen test result was positive; COPD, chronic obstructive pulmonary disease; CXR, chest radiograph.

*Data are given as number (percentage) of each group unless otherwise indicated.

†Data are given as mean ± SD.

biotic group carried a clinical admitting diagnosis of pneumonia more often than the no-antibiotic group.

Of the 150 physician surveys mailed, 97 (65%) were returned. The primary reason for continuing an antibiotic was concern about secondary bacterial infection (60 [62%]), followed by patient improvement on the community-acquired pneumonia pathway (26 [27%]). Physicians were not very concerned about the validity of the CXR report (7 [7%]) or the accuracy of the rapid influenza test result (0%), and the need to justify the hospitalization by using intravenous antibiotics was chosen in only 4 (4%) cases. Other concerns included liability, patient comorbidities, and family wishes. Of the 24 physicians who chose more than 1 reason for continuing antibiotics, 18 (75%) listed concern for bacterial infection as the primary issue. Of 97 respondents, 17 (18%) claimed they would discontinue antibiotic therapy, which was not significantly ($P=.85$) different than the actual result of 12 (14%) noted by medical record review. Approximately two thirds of physicians believed that negative or normal available test results (white blood cell count, CXR result, or blood and sputum bacterial culture result) would be sufficient to discontinue antibiotic therapy. Approximately one quarter of those surveyed believed additional new diagnostic tests to rule out bacterial infections and/or practice guidelines would be helpful in conjunction with routine tests. Of the 92 physicians who responded, 56 (61%), 29 (32%), and 7 (8%) would accept a 5% or less, 10% or less, and 20% or less chance of bacterial infection risks, respectively, before discontinuing antimicrobial therapy. (Five [5%] of the 97 surveys had no answer for the last question.)

Our study demonstrates a significant reduction in antibiotic use in hospitalized adults with positive rapid influenza test results compared with those in whom the influenza diagnosis was delayed. These data are encouraging, in that indiscriminate antibiotic use can be curtailed with the timely diagnosis of viral respiratory infection in hospitalized adults. Our study is limited by its retrospective nature because the different clinical characteristics of Ag+ and Ag0 groups undoubtedly affected patient management, complicating assessment of the impact of the rapid test results. However, rapid antigen status was independently associated with withholding or discontinuing antibiotics in multivariate analysis, providing evidence that the test results were affecting management.

Our data are consistent with those of several retrospective studies¹⁰⁻¹³ examining the effect of influenza testing in febrile children, demonstrating significant reductions in antibiotic use and other benefits among Ag+ patients. Before the widespread availability of rapid influenza testing, Bonner et al¹⁰ demonstrated that physician knowledge of rapid diagnostic test results led to significant changes in decision making. Children who were Ag+ were randomized to having the information withheld or available to the treating physician. Significant reductions in antibiotic use, ancillary testing, and length of hospital stay were demonstrated in the group in which positive influenza test results were known. Although the impact of rapid influenza testing might be expected to yield different results in hospitalized adults because most are elderly patients with multiple chronic medical conditions, our data suggest that a beneficial effect of reduced antibiotic use can also be demonstrated in older patients. Data regarding the value of rapid influenza testing in adults have previously been limited to studies¹⁶ in long-term care facilities and on antiviral prophylaxis. In 1 small observational study¹⁷ of 15 elderly patients hospitalized with influenza, investigators demonstrated a decrease in hospital stay from a mean of 11 days to 8 days after rapid viral testing was implemented at the hospital.

Although it is encouraging that antibiotic use was reduced in patients who were Ag+, 61% (27/44) of those deemed at low risk for bacterial infection continued to receive antibiotics despite their rapid influenza diagnosis. Patients who continued to receive antibiotics were more often older, were smokers with higher rates of underlying chronic obstructive pulmonary disease, and had abnormal lung examination results. These trends suggest that physicians were not indiscriminate with their therapy but rather responding to a perceived increased risk of bacterial infection in an older and frailer group. Bacterial and viral causes of chronic obstructive pulmonary disease exacerbations are well described and may be challenging to differentiate.¹⁸⁻²⁰ In addition, numerous studies²¹⁻²⁷ demonstrate in vitro bacterial-viral synergy, and high rates of bacterial pneumonia have been documented during influenza pandemics. Unfortunately, the precise risk of bacterial complications of influenza in older adults during periods of interpandemic influenza is difficult to ascertain. Bacterial complication rates during influenza infection have

been reported to range from 13% to 36% in observational studies,²⁸⁻³² but prospective investigations have yet to be done. To our knowledge, there are no data to support the use of antibiotics as a method of preventing influenza-related complications in healthy adults or in those with comorbidities.^{33,34}

Positive rapid influenza tests clearly resulted in increased antiviral use. Although the sensitivity of the rapid test is approximately 60% in hospitalized adults,¹⁵ empirical use of antiviral agents is uncommon, even during epidemic periods, as evidenced in our study. Thus, it is possible that a false-negative test result may dissuade physicians from appropriately prescribing antiviral agents in some patients. Notably, 39% of patients treated in this study presented outside the 48-hour therapeutic window recommended for prescribing antiviral therapy. There are limited data on the use of antiviral agents for the treatment of complicated influenza in hospitalized patients.^{35,36} Because a substantial viral load is needed to generate a positive antigen test result, some authorities believe treatment of such patients is reasonable. Clearly, further studies are needed to address these issues.

Rapid influenza testing may affect changes in individual patient management, but routine rapid testing and isolation of infected patients may have broader benefits, such as reducing nosocomial influenza rates. More than half the influenza cases identified in this study resulted from hospital screening rather than physician testing. Nosocomial influenza not only results in patient suffering but also in increased health care costs, with the average extra charge per patient of approximately \$3800 noted in one study.³⁷

Given the environment of increasingly severe antibiotic-resistant nosocomial infections, control of inappropriate antibiotic use is highly desirable. With ever more sophisticated tools, such as RT-PCR and microarrays, rapid accurate diagnosis for a wide number of viral pathogens will become available in the near future.⁸ To optimize use of these new diagnostic tools and limit antibiotic use in patients with viral infection, more accurate methods of diagnosing concomitant bacterial infections are needed. Although two thirds of the respondents to our physician survey believed they would be comfortable discontinuing antibiotic therapy in patients with negative bacterial culture and CXR results, medical record review revealed that this was not the case. New tools, such as cellular proteomics and soluble biomarkers, may help supplement traditional blood and sputum cultures to achieve this goal.^{38,39}

In conclusion, our data suggest that the use of rapid antigen testing results in a modest reduction in antibiotic use in adults hospitalized with influenza infection. Antibiotic use remains high despite diagnosis of influenza primarily because of physician concerns about secondary bacterial infections. Further research is needed to assess rates of concomitant bacterial infection during viral respiratory illness and to develop accurate methods for distinguishing viral from bacterial processes.

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