Aetna considers rapid diagnostic tests for viral influenza (e.g., Directigen Flu A, Directigen Flu A+B, Flu OIA, Quickvue Influenza Test, and Z Stat Flu) medically necessary.

See also CPB 0035 - Influenza Vaccine.

Background

In the context of an epidemic, the clinical diagnosis of influenza in a patient with fever, malaise, and respiratory symptoms can be made with some certainty. In the absence of an epidemic of influenza, however, the diagnosis may be uncertain. In these cases, rapid diagnostic tests (which take less than 1 hour to perform) may be helpful in distinguishing influenza from infection with a number of other viruses (and occasionally streptococcal pharyngitis) that produce headache, muscle aches, fever, and/or cough. The results of these rapid diagnostic tests for influenza may be useful in
selecting appropriate antiviral therapy, avoiding inappropriate antibiotic therapy, and in promptly initiating measures to decrease the spread of disease.

Most of the rapid diagnostic tests that can be done in a physician's office are approximately greater than 70% sensitive for detecting influenza and approximately greater than 90% specific (CDC, 2005). Thus, as many as 30% of samples that would be positive for influenza by viral culture may give a negative rapid test result. In addition, some rapid test results may indicate influenza when a person is not infected with influenza.

Guidelines from the Centers for Disease Control and Prevention (CDC) (Harper et al, 2005) explain that commercial rapid diagnostic tests can detect influenza viruses within 30 mins. Some tests are approved for use in any outpatient setting, whereas others must be used in a moderately complex clinical laboratory. These rapid tests differ in the types of influenza viruses they can detect and whether they can distinguish between influenza types. Different tests can detect: (i) only influenza A viruses; (ii) both influenza A and B viruses, but not distinguish between the 2 types; or (iii) both influenza A and B and distinguish between the two.

Centers for Disease Control and Prevention guidelines explain that none of the tests provide any information about influenza A subtypes. The types of specimens acceptable for use (i.e., throat, nasopharyngeal, or nasal aspirates, swabs, or washes) also vary by test. The specificity and, in particular, the sensitivity of rapid tests are lower than for viral culture and vary by test. The CDC recommends that, because of the lower sensitivity of the rapid tests, physicians should consider confirming negative tests with viral culture or other means because of the possibility of false-negative rapid test results, especially during periods of peak community influenza activity. In contrast, false-positive rapid test results are less likely, but
can occur during periods of low influenza activity. Therefore, when interpreting results of a rapid influenza test, physicians should consider the positive- and negative-predictive values of the test in the context of the level of influenza activity in their community (Harper et al, 2005). Package inserts and the laboratory performing the test should be consulted for more details regarding use of rapid diagnostic tests.

Centers for Disease Control and Prevention guidelines state that, despite the availability of rapid diagnostic tests, collecting clinical specimens for viral culture is critical, because only culture isolates can provide specific information regarding circulating strains and subtypes of influenza viruses. The guidelines explain that this information is needed to compare current circulating influenza strains with vaccine strains, to guide decisions regarding influenza treatment and chemoprophylaxis, and to formulate vaccine for the coming year. Virus isolates also are needed to monitor the emergence of antiviral resistance and the emergence of novel influenza A subtypes that might pose a pandemic threat.

Although widely used in emergency departments and physicians’ offices, antigen-based rapid assays have shown poor sensitivity for the H1N1 virus compared with culture or molecular diagnostic techniques. Drexler et al (2009) found only 11% sensitivity of a rapid antigen test with reverse transcription polymerase chain reaction (RT-PCR). Investigators compared the sensitivity of a commercially available antigen-based rapid test (BinaxNOW Influenza A & B Rapid Test) with that of a real-time RT-PCR (rRT-PCR) assay specific for the hemagglutinin gene of the 2009 H1N1 virus. Of 1,838 clinical specimens tested, 221 were confirmed as H1N1 positive by RT-PCR. When 144 of these PCR-positive specimens were evaluated using the rapid-antigen test, results were positive for only 16 (11.1%). The "gold standard" PCR also demonstrated poor sensitivity, detecting the 2009 H1N1
virus in just 12% of 1,838 respiratory specimens submitted at a time when this virus was pandemic and probably responsible for most influenza-like illness.

During May 2009, a few weeks after 2009 pandemic influenza A (H1N1) infection was first detected in the United States, outbreaks among students from 2 schools were detected in Greenwich, Connecticut (CT). Staff members from Greenwich Hospital and the CT Department of Public Health collected data on symptoms for 63 patients and submitted nasopharyngeal washings for testing using a rapid influenza diagnostic test (RIDT) for influenza A and B and rRT-PCR assay, thus affording an opportunity to assess the field performance of the RIDT. A total of 49 patients had infections with pandemic H1N1 confirmed by rRT-PCR (CDC, 2009). The findings of this performance assessment indicated that, compared with rRT-PCR, the sensitivity of the RIDT for detecting infection in patients with 2009 pandemic H1N1 was 47%, and the specificity was 86%. Sensitivity and specificity did not vary markedly by the presence or absence of CDC-defined influenza-like illness (ILI) or by time from symptom onset to specimen acquisition. In this group of patients, although positive RIDT results performed well in predicting confirmed infection with pandemic H1N1 virus (positive predictive value: 92%), negative tests did not accurately predict the absence of infection (negative predictive value: 32%). These findings affirm recent CDC recommendations against using negative RIDT results for management of patients with possible 2009 pandemic H1N1 infection.

Hawkes et al (2010) examined the diagnostic accuracy of a RIDT and direct fluorescent antibody (DFA) assay for swine-origin H1N1 virus (S-OIV) by using rRT-PCR as the reference standard. These investigators prospectively recruited children (aged 0 to 17 years) assessed in the emergency department of a pediatric referral hospital and a community pediatric clinic for ILI between May 22 and July 25, 2009. RIDT (performed on-site) and DFA were compared with rRT-PCR to determine
their sensitivity and specificity for S-OIV. They also compared the sensitivity of RIDT for S-OIV to that for seasonal influenza over 2 preceding seasons. Of 820 children enrolled, 651 were from the emergency department and 169 were from the clinic. Sensitivity of RIDT was 62 % (95 % confidence interval [CI]: 52 % to 70 %) for S-OIV, with a specificity of 99 % (95 % CI: 92 % to 100 %). Sensitivity of DFA was 83 % (95 % CI: 75 % to 89 %) and was superior to that of RIDT (p < 0.001). Sensitivity of RIDT for S-OIV was comparable to that for seasonal influenza when using DFA supplemented with culture as the reference standard. Sensitivity of RIDT for influenza viruses was markedly higher in children 5 years of age or younger (p = 0.003) and in patients presenting less than or equal to 2 days after symptom onset (p < 0.001). The authors concluded that the sensitivity of RIDT for detection of S-OIV is higher than recently reported in mixed adult-pediatric populations but remains suboptimal.

Cruz and associates (2010) evaluated the performance of a RIDT in detecting H1N1 2009 influenza A virus in respiratory samples from pediatric patients in comparison to that of rRT-PCR and viral culture. Patients for whom the RIDT, viral culture, and rRT-PCR results were known were included. Sensitivity, specificity, and likelihood ratios (LRs) were calculated. A total of 3,030 specimens had RIDT results paired with both rRT-PCR and viral culture results. With rRT-PCR as the reference, overall test sensitivity was 45 % (95 % CI: 43.3 % to 46.3 %) and specificity was 98.6 % (95 % CI: 98.1 % to 99 %). Positive and negative LRs were 32.9 (95 % CI: 22.9 to 45.4) and 0.56 (95 % CI: 0.54 to 0.58), respectively. Sensitivity of RIDT was significantly higher in young infants and children younger than 2 years than in older children. Using viral culture as the reference standard, RIDT sensitivity was 55.5 % (95 % CI: 51.9 % to 59.6 %) and specificity was 95.6 % (95 % CI: 95 % to 96.1 %). The positive and negative LRs were 12.6 and 0.47, respectively. The authors concluded that the RIDT had relatively poor sensitivity but excellent specificity in this consecutive series of respiratory
specimens obtained from pediatric patients. Although a positive RIDT result was highly accurate in predicting infection with influenza type A H1N1 2009 in children, a negative RIDT result did not preclude a child having H1N1. Thus, for children at high-risk with ILI during high prevalence periods of influenza, empiric initiation of antiviral therapy should be considered for patients with a negative RIDT result.

Parida et al (2011) stated that the recent emergence of the S-OIV poses a serious global health threat. Rapid detection and differentiation of S-OIV from seasonal influenza is crucial for patient management and control of the epidemics. These researchers reported a 1-step, single-tube accelerated and quantitative S-OIV-specific H1 reverse transcription loop-mediated isothermal amplification (RTLAMP) assay for clinical diagnosis of S-OIV by targeting the H1 gene. A comparative evaluation of the H1-specific RTLAMP assay vis-a-vis the World Health Organization (WHO)-approved rRT-PCR, involving 239 acute-phase throat swab samples, demonstrated exceptionally higher sensitivity by picking up all of the 116 H1N1-positive cases and 36 additional positive cases among the negatives that were sequence-confirmed as S-OIV H1N1. None of the rRT-PCR-positive samples were missed by the RTLAMP system. The comparative analysis revealed that S-OIV RTLAMP was up to 10-fold more sensitive than the WHO rRT-PCR; it had a detection limit of 0.1 tissue culture infectious dosage of (50)/ml. One of the most attractive features of this isothermal gene amplification assay is that it seems to have an advantage in monitoring gene amplification by means of SYBR Green I dye-mediated naked-eye visualization within 30 mins compared to 2 to 3 hours for a eRt-PCR. This suggested that the RTLAMP assay is a valuable tool for rapid, real-time detection and quantification of S-OIV in acute-phase throat swab samples without requiring sophisticated equipment.
Su and colleagues (2012) applied the developed paired surface plasma waves biosensor (PSPWB) in a dual-channel biosensor for rapid and sensitive detection of S-OIV. In conjunction with the amplitude ratio of the signal and the reference channel, the stability of the PSPWB system is significantly improved experimentally. The theoretical limit of detection (LOD) of the dual-channel PSPWB for S-OIV is 30 PFU/mL (PFU, plaque-forming unit), which was calculated from the fitting curve of the surface plasmon resonance signal with a S-OIV clinical isolate concentration in phosphate-buffered saline (PBS) over a range of 18 to 1.8 x 10^6 PFU/mL. The LOD is 2 orders of magnitude more sensitive than the commercial rapid influenza diagnostic test at worst and an order of magnitude less sensitive than rRT-PCR whose LOD for S-OIV in PBS was determined to be 3.5 PFU/mL in this experiment. Furthermore, under in-vivo conditions, this experiment demonstrates that the assay successfully measured S-OIV at a concentration of 1.8 x 10^2 PFU/mL in mimic solution, which contained PBS-diluted normal human nasal mucosa. Most importantly, the assay time took less than 20 mins. The authors concluded that from these findings, the dual-channel PSPWB potentially offers great opportunity in developing an alternative PCR-free diagnostic method for rapid, sensitive, and accurate detection of viral pathogens with epidemiological relevance in clinical samples by using an appropriate pathogen-specific antibody.

Additional information concerning diagnostic testing for influenza is available at

Clinical Description and Lab Diagnosis of Influenza
(http://www.cdc.gov/flu/professionals/diagnosis/)

CPT Codes / HCPCS Codes / ICD-10 Codes
Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

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<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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<tr>
<td></td>
<td>CPT codes covered if selection criteria are met:</td>
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<tr>
<td></td>
<td>87804 Infectious agent antigen detection by immunoassay with direct optical observation; influenza</td>
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<td>ICD-10 codes covered if selection criteria are met:</td>
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<tr>
<td></td>
<td>B34.9 Viral infection, unspecified</td>
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<td></td>
<td>J10.00 - J11.89 Influenza due to other influenza virus</td>
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<td>R05 Cough</td>
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<td>R05.9 Fever, unspecified</td>
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<td>R06.02 Shortness of breath</td>
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<td>R51 Headache</td>
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<td>R53.81 Other malaise</td>
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The above policy is based on the following references:


37. Munoz FM. Seasonal influenza in children: Clinical features and diagnosis. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed March 2015.


AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0476 Influenza Rapid Diagnostic Tests

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania new 11/01/2018