Published in final edited form as:

J Clin Virol. 2014 September ; 61(1): 176–177. doi:10.1016/j.jcv.2014.05.016.

Response to Al-Husayni and Hassoun

Timothy M. Uyeki[*] **Daniel B. Jernigan**

Influenza Division, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, GA, United States

Keywords

Influenza; Influenza diagnostic testing; Antiviral treatment

To the Editor,

Al-Husayni and Hassoun state that "CDC recommendations for diagnosis and plan of treatment do not reflect latest advances in diagnostic methods and lack emphasis on antimicrobial stewardship and infection prevention in the healthcare setting," argue for RT-PCR to be the initial influenza test performed, and object to empiric antiviral treatment of influenza [1]. Unfortunately, they have misinterpreted CDC guidance and clarification is indicated.

RT-PCR is the most accurate influenza test and is recommended, especially in hospitalized patients with pneumonia and suspected influenza [2–4]. In ambulatory settings, RT-PCR is generally not available and timely results may not be available to inform clinical management. In some hospitals, influenza RT-PCR testing is a send-out test with results taking one day or longer. CDC provides guidance to clinicians and public health on the strengths and limitations of available influenza tests and how to properly interpret results [2,5]. CDC recognizes that many clinicians use rapid influenza diagnostic tests (RIDTs); however, CDC provides guidance recommending caution on their use, and states the disadvantages of RIDTs: "sub-optimal test sensitivity, false negative results are common, especially when influenza activity is high" [5].

CDC recommends empiric antiviral treatment with a neuraminidase inhibitor (NAI) (oral oseltamivir or inhaled zanamivir) as soon as possible for any outpatient in a group at higher risk for complications from influenza or for any hospitalized patient with suspected or confirmed influenza [6]. This is because (1) RIDTs lack sensitivity to detect influenza viruses in upper respiratory tract specimens compared to RT-PCR [7]; (2) the priority is to

[*]Corresponding author. Tel.: +1 404 639 0277; fax: +1 404 639 3866. tuyeki@cdc.gov (T.M. Uyeki).

Competing interests
None declared.

Disclaimer
This manuscript represents the views of the authors and not the official policy of the Centers for Disease Control and Prevention.

Ethical approval
Not applicable.

treat those at highest risk for developing more severe disease and hospitalizations; and (3) observational studies of hospitalized influenza patients indicate that early initiation of antiviral treatment provides the greatest clinical benefit, especially for influenza A(H1N1)pdm09 virus infection [8–10].

The authors claim that providing antiviral treatment to patients without influenza can lead to "greater risk of toxicity, adverse effects and antiviral or anti-bacterial resistance," and that increased use of NAI's "increases the likelihood of antiviral resistance development" [1]. Whereas inappropriate antibacterial use can lead to emergence of antibiotic resistance by host bacteria, there is no impact of antiviral treatment upon antiviral resistance if the patient does not have influenza. The increase in oseltamivir resistance to seasonal influenza A(H1N1) viruses during 2007–2009 was linked to increased transmissibility of resistant strains unrelated to use of NAI's [11]. High prevalence of oseltamivir-resistant seasonal H1N1 viruses was first noted in Scandinavian countries with low oseltamivir usage whereas low prevalence of oseltamivir resistance was observed in Japan where oseltamivir treatment for influenza has been widespread for many years. Sporadic cases of oseltamivir-resistant H1N1pdm09 virus infection have been detected, including in some nosocomial outbreaks; however, the prevalence of circulating oseltamivir-resistant H1N1pdm09 virus remains low [12].

CDC infection prevention guidance for seasonal influenza in healthcare settings emphasizes standard and droplet precautions and isolation or cohorting of symptomatic patients with suspected or laboratory-confirmed influenza [13]. Implementation of such measures should not be delayed while testing results are pending, and can be beneficial for preventing spread of other respiratory viruses that also cause influenza-like illness.

References

[1]. Al-Husayni N, Hassoun A. Making the case for RT-PCR for the diagnosis of H1N1. J Clin Virol 2014.

[2]. CDC. Guidance for Clinicians on the Use of RT-PCR and Other Molecular Assays for Diagnosis of Influenza Virus Infection. Available at: http://www.cdc.gov/flu/professionals/diagnosis/molecular-assays.htm

[3]. Uyeki TM. Preventing and controlling influenza with available interventions. N Engl J Med 2014;370(2 (9)):789–91. [PubMed: 24450860]

[4]. Napolitano LM, Angus DC, Uyeki TM. Critically ill patients with influenza A(H1N1)pdm09 virus infection in 2014. JAMA 2014;311(Aprii (13)):1289–90. [PubMed: 24566924]

[5]. CDC. Guidance for Clinicians on the Use of Rapid Influenza Diagnostic Tests. Available at: http://www.cdc.gov/flu/professionals/diagnosis/clinician.guidance_ridt.htm

[6]. CDC. Influenza Antiviral Medications: Summary for Clinicians. Available at: http://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

[7]. Chartrand C, Leeflang MM, Minion J, Brewer T, Pai M. Accuracy of rapid influenza diagnostic tests: a meta-analysis. Ann Intern Med 2012;156(4 (7)):500–11. [PubMed: 22371850]

[8]. Muthuri SG, Venkatesan S, Myles PR, Leonardi-Bee J, Al Khuwaitir TSA, Al Mamun A, et al. Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data. Lancet Respir Med 2014;(3), 10.1016/S2213-2600(14)70041-4.

[9]. Louie JK, Yang S, Samuel MC, Uyeki TM, Schechter R. Neuraminidase inhibitors for critically ill children with influenza. Pediatrics 2013;132(12 (6)):e1539–45, 10.1542/peds.2013-2149. [PubMed: 24276847]

[10]. Hsu J, Santesso N, Mustafa R, Brozek J, Chen YL, Hopkins JP, et al. Antivirals for treatment of influenza: a systematic review and meta-analysis of observational studies. Ann Intern Med 2012;156(4 (7)):512–24. [PubMed: 22371849]

[11]. Lackenby A, Thompson CI, Democratis J. The potential impact of neuraminidase inhibitor resistant influenza. Curr Opin Infect Dis 2008;21(12 (6)):626–38. [PubMed: 18978531]

[12]. Hurt AC, Chotpitayasunondh T, Cox NJ, Daniels R, Fry AM, Gubareva LV, et al. WHO Consultation on Pandemic Influenza A (H1N1) 2009 Virus Resistance to Antivirals. Antiviral resistance during the 2009 influenza A H1N1 pandemic: public health, laboratory, and clinical perspectives. Lancet Infect Dis 2012;12(3 (3)):240–8. [PubMed: 22186145]

[13]. CDC. Prevention Strategies for Seasonal Influenza in Healthcare Settings. Guidelines and Recommendations. Available at: http://www.cdc.gov/flu/professionals/infectioncontrol/healthcaresettings.htm