LAB NEWS

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Characterization of Influenza A H1 and H3 Subtypes by RT-PCR and Prediction of Resistance to Oseltamivir

In December 2008, based on data indicating a high prevalence of influenza A (H1N1) virus strains resistant to oseltamivir (Tamiflu), the CDC issued interim recommendations for antiviral treatment and chemoprophylaxis of influenza during the 2008-09 influenza season (see **Table**). When influenza A (H1N1) virus infection or exposure is suspected, zanamivir, or a combination of oseltamivir and rimantadine or amantadine, are more appropriate options than oseltamivir alone. A summary table (modified for YNHH) of the CDC recommendations is presented below; for the full content of the CDC recommendations, see http://www.cdc.gov/flu/professionals/antivirals/index.htm.

Influenza A Subtype RT-PCR at YNHH: To aid in selecting antiviral drugs, the Clinical Virology Laboratory has set up the CDC assay for characterization of influenza A positives as H1 or H3 by RT-PCR (*CDC Realtime RT-PCR Protocol for Detection and Characterization of Influenza)*.

This assay was originally devised to monitor for emergence of a new influenza pandemic hemagglutinin subtype, and thus does not target the neuraminidase gene. Rather it is presumed, based on currently circulating subtypes, that H1 detection indicates H1N1, and H3 detection indicates H3N2.

Test indication:
Influenza A subtype RT-PCR should be ordered only if the patient is to be treated with a neuraminidase inhibitor.

Test ordering and availability: In general, an influenza A-positive sample on the patient will already be available in the laboratory. Therefore, to order a subtype, **send a fax** to the Virology Laboratory (**fax: 688-8177)** with the patient's name and MRN requesting the addition of an influenza subtype.

Note: Influenza A H1/H3 RT-PCR will be done once a day, Mon-Fri. In the future, an automatic fax triggered by an order for Tamiflu may be implemented, but is not currently available.

Table: Interim Recommendations for the Selection of Antiviral Treatment Using Laboratory Test Results and Viral Surveillance Data, United States, 2008-09 season‡ *(modified according to drugs available at YNHH)*

Rapid antigen or other laboratory test	Predominant virus(es) in community	Preferred medication	Alternative (combination antiviral treatment)
Not done or negative, but clinical suspicion for influenza	**H1N1** or unknown	Zanamivir*	**Oseltamivir + Amantadine****
Not done or negative, but clinical suspicion for influenza	H3N2 or B	Oseltamivir	None
Positive A	**H1N1** or unknown	Zanamivir*	**Oseltamivir + Amantadine****
Positive A	H3N2 or B	Oseltamivir	None
Positive B	Any	Oseltamivir	None

* Zanamivir is not available at YNHH. Therefore, alternative combination therapy should be used.

** Rimantadine has fewer side effects than amantadine, but is not available at YNHH. Human data are lacking to support the benefits of combination antiviral treatment of influenza; however, these interim recommendations are intended to assist clinicians treating patients who might be infected with oseltamivir-resistant influenza A (H1N1) virus.

‡ Influenza antiviral medications used for treatment are most beneficial when initiated within the first two days of illness. Clinicians should consult the package insert of each antiviral medication for specific dosing information, approved indications and ages, contraindications/warnings/precautions, and adverse effects.

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