



COMMONWEALTH of VIRGINIA

Department of Health

P O BOX 2448
RICHMOND, VA 23218

KAREN REMLEY, MD, MBA, FAAP
STATE HEALTH COMMISSIONER

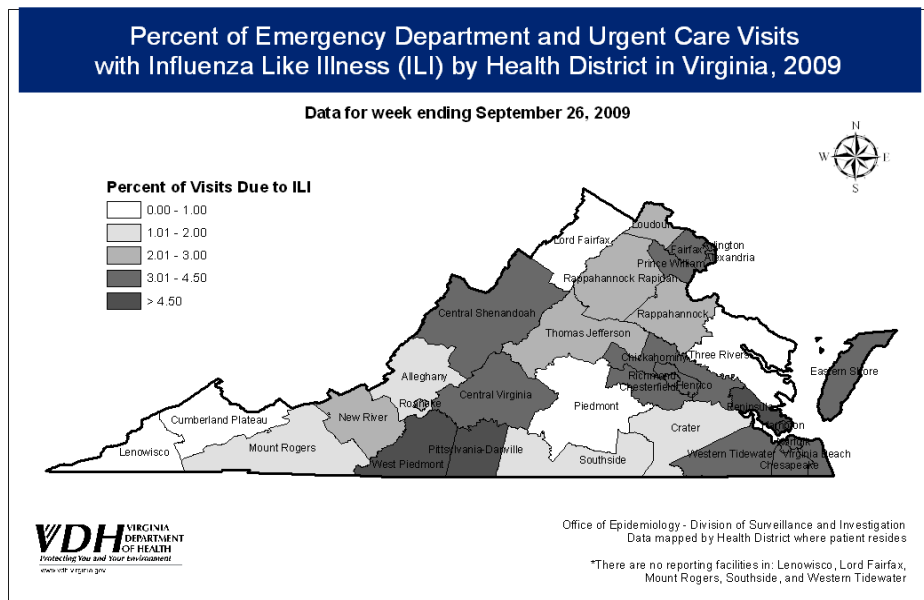
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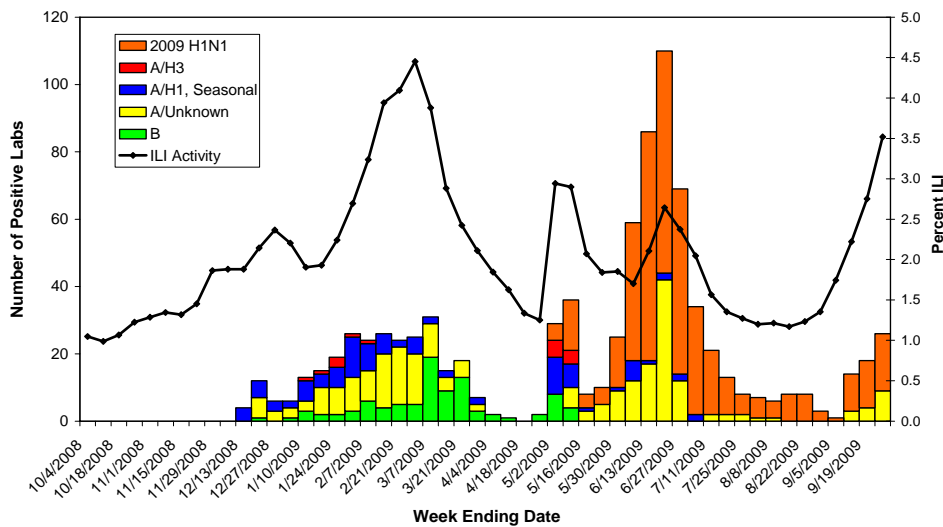
Dear Colleague:

I'm writing you this week to update you on where we stand in Virginia with the current influenza pandemic and to share some information that I believe can be helpful to you and your patients.

According to **Surveillance** reports, influenza activity is now approaching the level typically seen at the height (usually around February) of seasonal flu. Activity continues to be widespread in Virginia. Public Health sampling continues to demonstrate H1N1 as the predominate type.



Positive Laboratory Isolates and ILI Reports by Week in Virginia,
2008-2009 Influenza Season



The Virginia Department of Health (VDH) will be launching a **Communication** campaign to promote novel H1N1 vaccination in a few weeks, when the vaccine becomes available to the general public. The public can receive information about vaccine and novel H1N1 now at our website www.vdh.virginia.gov, through our VDH Inquiry Center at 1-877-ASK-VDH3 or by e-mailing questions to PHIC@vdh.virginia.gov. Technical information and consultation for the medical community is available by contacting your local health department or district health director. The VDH Division of Immunization at (804) 864-8055 also provides information on both general novel H1N1 vaccination questions; technical support for novel H1N1 vaccinators is also available at 866-866-375-9795.

The Centers for Disease Control and Prevention (CDC) has published updated pediatric antiviral dosing syringe and compounding information (see below) to assist you in **Direct Clinical Care**. This can be of help if you find that pediatric suspensions of antiviral medication are temporarily not available to you. Mindful of the potential for severe disease in pregnant women, I also want to encourage you to discuss the need for novel H1N1 vaccination with all pregnant women you treat. Initiation of antiviral medications should be started immediately in symptomatic pregnant women and not withheld pending laboratory results or in the face of negative rapid flu test results, given the low sensitivity of this test.

Community Mitigation activities are focused primarily on our K-12 schools as several school systems currently have increased absenteeism attributed to influenza. School closure has not been found to be an effective means of influenza control, but is considered if absenteeism affects the school's ability to function. To date, Virginia has had no school closures associated with novel H1N1 this fall. VDH staff work closely with schools facing increased influenza-related absenteeism to help them decrease the spread of disease through, for instance, decreasing student mingling (postponing dances, cancelling club meetings).

Hospitals across the state are discussing implementation of restricted visitation policies, limiting children coming to the facility. We are fully in support of these activities centered on protecting high risk patients from potential exposure.

The first very small shipment (43,500 doses) of novel H1N1 vaccine will be arriving in Virginia next week. Our initial **Vaccination** effort for this small initial shipment of live, attenuated influenza virus

(LAIV or “nasal mist”), is aimed at beginning to vaccinate health care and EMS workers and to validate the distribution system. This LAIV will be provided to hospitals and local health departments to begin this important vaccination process. Larger, routine shipments that will include injectable vaccine will be commencing shortly. These later shipments will go to medical providers, clinics, and other vaccinators and will be focused on assuring vaccine is available first for the priority groups identified by the CDC. Vaccine will be available to the general public once the priority groups have had the chance to be immunized. **VDH is dedicated to assuring that everyone who wishes to protect themselves with a novel H1N1 vaccination will have that opportunity.**

I understand that the main focus of the medical community is direct clinical care and during this time of medical surge this is certainly will continue to be your main focus. I appreciate anything you can do to help with vaccination and am impressed by the large number of medical practices, hospitals, and clinics that are incorporating novel H1N1 vaccination into their activities. Recognizing the need to support the VDH and CDC reporting requirements, VDH is exploring offering up to \$1,000 per vaccinating entity through our federal grant to defray the cost of initial efforts to register and begin VIIS usage. I will provide more information about this opportunity when it is available.

While the novel H1N1 vaccine is being manufactured in the same way as that used for the seasonal flu vaccine and it will be available in the same forms as seasonal flu vaccine, safety questions continue to be asked. Appended to my letter is a VDH Fact Sheet on Guillain-Barré syndrome (GBS).

Pandemics are rare but inevitable events that draw upon all our resources. I am proud to be joined with all of you as we work our way through this! Thank you for all your knowledge, dedication and compassion.

Sincerely,

A handwritten signature in cursive script, appearing to read "Karen Remley".

Karen Remley, MD, MBA, FAAP
State Health Commissioner

Updated Pediatric Antiviral Dosing Syringe and Compounding Information for 2009 H1N1 and Seasonal Flu

Background

As of September 25, 2009 influenza activity is increasing in the United States with 26 states reporting widespread influenza activity. So far, ninety-nine percent of all subtyped influenza viruses being submitted to CDC are 2009 influenza A (H1N1) viruses.

The current situation will likely affect pharmacies as a greater number of people than usual seek to fill prescriptions for influenza antiviral drugs or antibiotics to treat secondary bacterial infections, in addition to seeking advice on over-the-counter flu medications. This may affect supplies and availability of antiviral medications and other materials that may be needed to fill prescriptions.

Pharmacists and physicians who care for pediatric patients should be aware of two issues: (1) the possible need to compound Tamiflu® on site if commercially manufactured pediatric oral suspension formulation is not available, and (2) the need to ensure that the units of measure on the dosing dispenser and the dosing instructions match.

These situations are addressed in the updated interim recommendations issued by CDC on September 22, 2009 for the use of antivirals in the treatment and prevention of influenza which can be found at <http://www.cdc.gov/H1N1flu/recommendations.htm> and in the 2009-2010 Influenza Season: Information for Pharmacists available at http://www.cdc.gov/H1N1flu/pharmacist/pharmacist_info.htm.

Alternatives to Tamiflu® Oral Suspension for Pediatric Patients

If pediatric formulations of Tamiflu are not available, pharmacists may compound Tamiflu® 75 mg capsules into an oral suspension onsite. For the FDA -approved instructions for the emergency compounding of an oral suspension from Tamiflu® 75mg capsules, see the FDA approved manufacturer package insert for oseltamivir (Tamiflu), available on the FDA Web site at <http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM147992.pdf>

Compounding an oral suspension from Tamiflu® 75mg capsules provides an alternative when commercially manufactured oral suspension formulation is not readily available. Tamiflu® capsules 75 mg may be compounded using either of two vehicles: Cherry Syrup (Humco®) or Ora-Sweet® SF (sugar-free) (Paddock Laboratories). Other supplies needed to compound include mortar and pestle and amber glass or amber polyethyleneterephthalate (PET) bottle.

In addition, for children who may not be able to swallow capsules, Tamiflu® (30mg, 45mg and 75mg) capsules may be opened and mixed with sweetened liquids, such as regular or sugar-free chocolate syrup, if oral suspension is not available.

Note on Tamiflu Oral Suspension Syringe

The second issue that pharmacists and physicians may face is the need to ensure that the units of measure on the dosing dispenser and the dosing instructions match. An oral dosing dispenser with 30 mg, 45 mg, and 60 mg graduations of Tamiflu® is provided in the packaging for the manufacturer's product rather than graduations in milliliters (mL) or teaspoons (tsp). This can lead to patient or caregiver confusion and dosing errors. When dispensing commercially manufactured Tamiflu® oral suspension, pharmacists should ensure the units of measure on the dosing instructions match the dosing device provided. If prescription instructions specify administration using mL or tsp, then the device included in the Tamiflu® product package should be removed and replaced with an appropriate measuring device, such as an oral syringe if the prescribed dose is in milliliters (mL). When dispensing Tamiflu® oral suspension for children younger than 1 year of age, the oral dosing dispenser that is included in the product package should always be removed. Pharmacists and health care providers should provide an oral syringe that is capable of accurately measuring the prescribed milliliter (mL) dose, and counsel the caregiver how to administer the prescribed dose. Oseltamivir is authorized for emergency use in children younger than 1 year of age under an Emergency Use Authorization (EUA) issued by FDA. For the EUA, see <http://www.cdc.gov/h1n1flu/eua/pdf/tamiflu-hcp.pdf>.

For More Information:

2009-2010 Influenza Season: Information for Pharmacists: http://www.cdc.gov/H1N1flu/pharmacist/pharmacist_info.htm

Updated Interim Recommendations for the Use of Antiviral Medications in the Treatment and Prevention of Influenza for the 2009-2010 Season: <http://www.cdc.gov/H1N1flu/recommendations.htm>

Questions & Answers: Antiviral Drugs, 2009-2010 Flu Season: <http://www.cdc.gov/h1n1flu/antiviral.htm>

Updated Interim Recommendations for Obstetric Health Care Providers Related to Use of Antiviral Medications in the Treatment and Prevention of Influenza for the 2009-2010 Season:
http://www.cdc.gov/H1N1flu/pregnancy/antiviral_messages.htm

Antiviral Drugs: Summary of Side Effects: <http://www.cdc.gov/flu/protect/antiviral/sideeffects.htm>

For the FDA page on antiviral influenza drugs:
<http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm100228.htm>

For the FDA-approved package insert with instructions for the emergency compounding of an oral suspension from Tamiflu® 75mg capsules see <http://www.fda.gov/downloads/Drugs/DrugSafety/InformationbyDrugClass/UCM147992.pdf>

For the FDA public health alert regarding Tamiflu (oseltamivir) for Oral Suspension: Potential Medication Errors see <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm183714.htm>.

For additional information, you can also call CDC's toll-free hotline, 800-CDC-INFO (800-232-4636) TTY: (888) 232-6348, which is available 24 hours a day, every day.

THE NOVEL H1N1 INFLUENZA VACCINE AND THE RISK OF GUILLAIN-BARRÉ SYNDROME

Although uncommon, GBS enjoys relatively wide public recognition, in large part because of the attention cases received in the aftermath of the 1976 swine influenza vaccination campaign. In this fact sheet, we review GBS; highlight actions the Virginia Department of Health (VDH) is taking to monitor pandemic flu vaccine safety; and suggest talking points for responding to patient questions about the new vaccine.

1976 SWINE FLU

In February 1976, a new influenza A strain, the A/NJ/76(H1N1) virus or “swine flu,” caused severe respiratory illness in 13 soldiers and 1 death at Fort Dix, NJ.¹ Since this virus was deemed similar to the Spanish flu virus that produced the 1918 pandemic and serologic testing indicated that person-to-person transmission had occurred among over 200 recruits, public health officials feared another pandemic and advised vaccinating the entire U.S. population. The mass vaccination campaign began in October 1976 even though no cases of swine flu were reported beyond Fort Dix and there was no sign of a pandemic. In December 1976, when more than 500 cases of GBS were reported following vaccination of 48 million Americans, the vaccination campaign was suspended. Analysis indicated an elevated risk of GBS associated with receiving the 1976 flu vaccine, with one additional case of GBS per 100,000 persons vaccinated. This causal association is unique to the vaccine used in 1976, and studies of influenza vaccines used in subsequent years have found small or no increased risk of GBS.²

GUILLAIN-BARRÉ SYNDROME

GBS is an acute, bilateral and relatively symmetric weakness/paralysis of the limbs that may involve respiratory and cranial nerve-innervated muscles.³ The weakness/paralysis typically ascends from legs to arms. Initial symptoms may include pain, numbness, paresthesia, and/or weakness in the limbs. Deep tendon reflexes are decreased or absent in the affected limbs. The autonomic nervous system may be involved and lead to urinary retention, ileus, postural hypotension, sinus tachycardia, or even cardiac arrest. The death rate for GBS is about 4-15%. In most cases, the weakness reaches a peak between 12 hours and 28 days, followed by plateau and subsequent improvement. Electrophysiological studies are consistent with polyneuropathy, especially demyelinating patterns in North America and Europe, but studies done less than seven days after weakness onset may be normal. Cerebrospinal fluid classically demonstrates an elevated protein with a minimal increase in WBC. Treatment entails supportive care, and either IV immunoglobulin or plasma exchange. Despite modern treatment, up to 20% of survivors are disabled after one year.

THE EPIDEMIOLOGY OF GBS

GBS occurs worldwide at an annual incidence of 1-2 cases per 100,000. Men are 1.5 times more likely than women to develop GBS. Applying this rate to the population of Virginia, we would expect 80-160 new GBS cases annually. GBS incidence increases with age. Between 2000 and 2007, there were 68 GBS deaths in Virginia, 85% among those 60 years and older. Of note, those over 65 years are not among the priority groups for receiving the novel H1N1 influenza vaccine, unlike the seasonal flu vaccine.

INFLUENZA VACCINATION AND GBS

Multiple infectious illnesses, including *Campylobacter jejuni* and upper respiratory infections, are associated with GBS. It is important to remember that influenza infection itself may trigger GBS. One study estimated that influenza-related GBS was four to seven times higher than the risk of 1976 swine flu vaccine-associated GBS.⁴ No studies of influenza vaccine following the 1976 swine flu vaccine have demonstrated a substantial risk in GBS, and the current estimated risk of GBS based on the few positive studies is one additional case per 1 million persons vaccinated.⁵ According to the FDA/CDC Vaccine Adverse Events Reporting System (VAERS), there were seventeen GBS cases following influenza vaccination among Virginians from 1990-2008.[†] Influenza vaccine prevents serious illness, hospitalization, and death; these benefits outweigh any risk of GBS or other adverse events.

MONITORING VACCINE SAFETY

[†] Over 130 million doses of seasonal flu vaccine will be produced in 2009-2010. With that many Americans being vaccinated, cases of GBS following vaccination will occur by chance alone.

Results from clinical trials of the novel H1N1 influenza vaccine will be available soon. To date, there have not been reports of serious adverse events. Use of vaccine adjuvants is not anticipated in the U.S. The elements of the novel H1N1 virus included in the vaccine closely match the currently circulating novel H1N1 virus, and so the vaccine is predicted to work well in preventing infection and serious illness. Furthermore, the novel H1N1 influenza vaccine is produced in the same manner and believed to be as safe as the typical seasonal flu vaccine. Therefore, we are confident that this vaccine will be effective, safe, and will save the lives of those Virginians most vulnerable to infection, who are included among the priority groups for early vaccination.

VDH will monitor vaccine safety in several ways. First, we will put the benefits of vaccination in the context of the burden of disease by closely monitoring influenza-like illness in emergency departments and urgent care centers. During the 1976 swine flu, even a small risk of GBS was unacceptable given that the supposed pandemic never materialized. Not only has novel H1N1 already reached pandemic proportions and produced significant morbidity and mortality, but recent data also show that the burden of disease from novel H1N1 influenza is on the rise. Second, we will monitor administration of vaccine through a vaccine registry, the Virginia Immunization Information System (VIIS). Third, we are starting active surveillance for GBS. Health care providers are asked to report all GBS cases, regardless of vaccination status, to VDH using a simple one-page form.[‡] Finally, health care providers should report any adverse events following vaccination to VAERS (www.vaers.hhs.gov). Vaccine safety monitoring is a shared responsibility and we cannot do our job without the cooperation of clinicians on the front lines.

WHAT DO WE TELL PATIENTS?

Here are talking points that might be useful in discussions with your patients and their families

The risk of GBS following novel H1N1 influenza vaccination is unknown, but there is no evidence to suggest that the risk will be higher than for the seasonal influenza vaccine. You should avoid saying that the novel H1N1 influenza vaccine has “no risk.”

The benefits of novel H1N1 influenza vaccination will likely far exceed the risks. Although common sense prevention measures are also important, vaccination is the best means of preventing the flu and curbing its spread. Forgoing vaccination risks overburdening the healthcare delivery system and puts the most vulnerable populations at unnecessary risk. It is worth noting that the highest incidence of hospitalization to date has been among children less than 4 years of age.⁶

GBS has many causes, including infection from the influenza virus. The majority of GBS cases follow GI and respiratory infections, and the risk of developing GBS from the flu is likely to be higher than the risk of developing GBS from receiving the vaccine.

Lead by example. Nothing will allay the fears of your patients like hearing that you and your staff have been or will be vaccinated. Healthcare workers and emergency medical services personnel are among the priority groups[§] for early novel H1N1 influenza vaccination.⁷

RESOURCES

www.cdc.gov/h1n1flu
www.vdh.virginia.gov

ACKNOWLEDGEMENT

VDH thanks the Oregon Public Health Department for sharing their newsletter, which served as the template for this document.

REFERENCES

[‡] Download the GBS reporting form at <http://www.vdh.virginia.gov/Epidemiology/Surveillance/gbs.htm>.

[§] Pregnant women; people who live with or provide care for infants <6 months of age; health care and emergency medical services personnel; children and young adults aged 6 months–24 years; persons aged 25–64 years who have medical conditions that put them at higher risk for influenza-related complications.

- 1 Sencer DJ, Millar JD. Reflections on the 1976 swine flu vaccination program. *Emerg Infect Dis* 2006; 12:29–33.
- 2 Haber P, Sejvar J, Mikaeloff Y, et al. Vaccines and Guillain-Barré syndrome. *Drug Saf* 2009;32(4):309-23.
- 3 Hughes RA, Cornblath DR. Guillain-Barre syndrome. *Lancet* 2005;366:1653–1666.
- 4 Sivadon-Tardy V, Orlikowski D, Porcher R et al. Guillain-Barre syndrome and influenza virus infection. *Clin Infect Dis* 2009;48:48–56.
- 5 Centers for Disease Control and Prevention. Prevention and control of seasonal influenza with vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009. *MMWR* 2009;58 (No. RR-8):1–52.
- 6 Centers for Disease Control and Prevention. Novel H1N1 Flu: Facts and Figures. Available from www.cdc.gov/h1n1flu/surveillanceqa.htm (Accessed 09/24/2009)
- 7 Centers for Disease Control and Prevention. Use of influenza A (H1N1) 2009 monovalent vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009. *MMWR* 2009;58(No. RR-10):1–8.