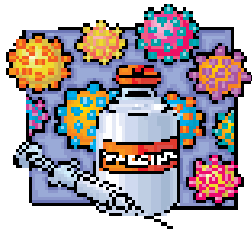




A PHARMACY CONTINUING EDUCATION PROGRAM

W-F Professional Associates, Inc. 400 Lake Cook Rd., Suite 207 Deerfield, IL 60015 847-945-8050

June 2010 "Overview 2009 H1N1 Epidemic" 707-000-10-006-H01-P



*This Month:
"Overview---2009
H1N1 Epidemic"*

ATTENTION!!



FAX # ERROR.

In the May 2010 lesson, a typo indicated an incorrect FAX #.

**The correct FAX # is
847-945-5037.**

**IF YOU FAXED ANY QUIZZES TO THE WRONG FAX
(847-947-5037), PLEASE RE-FAX THEM. WE APOLOGIZE.**

HAVE YOU RECENTLY MOVED? PLEASE NOTIFY US.

The 2009 H1N1 epidemic not only took most health professionals by surprise, it placed a huge responsibility on pharmacy practitioners. Is the concern over? Where do our pharmacy challenges continue? Our goal is to take a look at what occurred, and where things may go. This lesson provides 1.25 hours (0.125 CEUs) of credit, and is intended for pharmacists in all practice settings. **The program ID # for this lesson is 707-000-10-006-H01-P. Pharmacists completing this lesson by June 30, 2013 may receive full credit.**

To obtain continuing education credit for this lesson, you must answer the questions on the quiz (70% correct required), and return the quiz. Should you score less than 70%, you will be asked to repeat the quiz. Computerized records are maintained for each participant.

If you have any comments, suggestions or questions, contact us at the above address, or call toll free 1-800-323-4305. (In Alaska and Hawaii phone 1-847-945-8050). **Please write your ID Number (the number that is on the top of the mailing label) in the indicated space on the quiz page** (for continuous participants only).

The objectives of this lesson are such that upon completion the participant will be able to:

1. Describe the epidemiology, diagnosis & basic virology associated with the 2009 H1N1 epidemic.
2. List treatment options for the 2009 H1N1 virus.
3. Discuss the prevention strategies & vaccination recommendations for different age groups

All opinions expressed by the author/authors are strictly their own and are not necessarily approved or endorsed by W-F Professional Associates, Inc. Consult full prescribing information on any drugs or devices discussed.

BACKGROUND

The first cases of the novel swine-origin influenza A H1N1 virus were identified by the Centers for Disease Control and Prevention (CDC) on April 21, 2009. Two children from Southern California were found to have a febrile respiratory illness consistent with influenza A, but not identified as human H1N1, H3N2, or H5N1 subtypes. The viral isolates were genetically similar, resistant to adamantanes, and contained a unique combination of genes not previously reported in swine or human influenza viruses. The children did not have exposure to each other or swine, therefore indicating human to human transmission of the novel influenza A H1N1 virus. (1) Several days later, the CDC reported the same strain had been found in patients in Mexico.(2)

In response to these cases, increased surveillance was implemented by the Mexican Health Ministry and the World Health Organization (WHO). In June 2009, the WHO declared a global pandemic of influenza (H1N1). With almost 30,000 cases of the novel 2009 influenza (H1N1) virus in 74 countries, the WHO responded by declaring a phase 6 pandemic. This indicates human to human spread of the virus into at least 1 other country in a different WHO region in addition to human to human spread of the virus among 2 countries in 1 WHO region. This declaration was a reflection on the spread of the new virus, not the severity of illness. (3,4)

VIROLOGY

Influenza viruses belong to the *orthomyxoviridae* family, and are classified into three distinct types: influenza A, influenza B and influenza C. The basis for the distinct classification is the major antigenic differences. In addition, the three influenza types have differences such as genetic organization, structure, host range, epidemiology, and clinical characteristics. All three viruses share presence of a host-derived envelope, envelope glycoproteins (essential for viral entry and egress from cells), and a segmented genome of negative sense single-stranded RNA. (5,6) The nomenclature for influenza viruses is based on the type, geographical origin, strain designation and year of isolation. For example, the novel 2009 H1N1 virus was first isolated in California in 2009 and is identified as influenzaA/California/04/09 (H1N1). In addition, influenza A is further classified based on the hemagglutinin (H) and neuraminidase (N) activity. Influenza B and C do not have subtypes. Sixteen hemagglutinin and nine neuraminidase subtypes have been identified for influenza A of which only 3 H subtypes and 2 N subtypes have been implicated in human influenza disease. These include H1, H2, H3 and N1, N2 subtypes. (7) The H protein helps bind the virus to host receptor cells and subsequent fusion. Viral release from host cells is facilitated by the N proteins. (6)

Alteration of the antigen structure (also known as antigenic variation) through drift and shift of H and N proteins enable the virus to escape host defenses. Minor changes in the H and N antigens refer to antigenic drift. Antigenic drifts are associated with the annual changes in the influenza epidemic whereby reducing the effectiveness of the previous seasonal vaccine. The antigenic variation of influenza is one of its most remarkable features. Amino acid changes occur every 2-3 years that result in H and N protein changes and refers to an antigenic shift. (5, 6, 7)

Antigenic shift introduces an influenza subtype in which the population has no previous exposure and can result in influenza pandemics. In the twentieth century, there were three influenza pandemics. The first one was the "Spanish" flu of 1918 that resulted in up to 100 million deaths worldwide, with the death rate highest among young healthy adults. The second pandemic was "Asian" flu of 1957 which introduced H2N2 and resulted in 2 million deaths worldwide. The third pandemic was the "Hong Kong" flu of 1968 which resulted in 1 million deaths worldwide. (6)

The novel 2009 influenza (H1N1) was an unprecedented event that did not fit the classic definitions of antigenic shift or drift. Because H1N1 has been in continuous circulation since 1977, most people born before 1956 had some protective immunity, therefore, the development could not be explained by an antigenic shift. The 2009 influenza did not fit the definition of antigenic drift because it did not have evolutionary roots from previous human origin H1N1 influenza viruses. The 2009 influenza (H1N1) has genetic elements from swine, human, avian and Eurasian swine strains of influenza (H1N1). The 2009 H1N1 pandemic was unexpected. Its virulence was thought to be low compared to avian flu (H5N1). The H5N1 is highly lethal in a small number of patients and is inefficiently transmitted, whereas the novel influenza A has a high transmission rate, and led to the pandemic in early spring/summer of 2009. (6, 7)

CE PRN® (ISSN 0199-5006) is owned and published by W-F Professional Associates, Inc. 400 Lake Cook Road, Suite 207, Deerfield, Illinois 60015.

William J. Feinberg, President. CE PRN® is published eleven times per year, monthly, January through November. Subscription rate is \$110.00 per year. Second-Class Postage paid at Deerfield, Illinois 60015 and at additional mailing offices. © 2009 by W-F Professional Associates, Inc.

All rights reserved. None of the contents of this publication may be reproduced in any form without the written permission of the publisher.

POSTMASTER: Send all address changes to

W-F Professional Associates, Inc., 400 Lake Cook Road, Suite 207, Deerfield, IL 60015.

June 2010

EPIDEMIOLOGY

The novel 2009 influenza is transmitted from person to person through close contact. This is similar to seasonal influenza. It is transmitted by droplet exposure (when infectious droplets are projected onto mucous membranes), contact exposure (contaminated hands exposed to facial mucous membranes), and airborne exposure (by inhalation of infectious airborne particles). (6, 7, 8) The relative contribution of each mode of transmission is unknown and likely to be dependent on other factors. (7, 8)

Influenza can be detected year around, but infection rates peak during winter months. In the northern hemisphere, the peak influenza season is February, whereas in the southern hemisphere it peaks in June or July. The incubation period ranges from one to four days, but on average lasts 2 days. Influenza shedding begins the day before the illness (up to 5-7 days after initial infection). Viral shedding can last longer in young children and immunocompromised patients. The greatest amount of virus is shed during the first couple of days of illness. (8)

The majority of the cases of novel 2009 influenza occurred in people aged 18 to 64. Typically with seasonal influenza, people aged 65 years or greater have the majority of the complications and influenza related deaths. With the novel 2009 H1N1, over 85% of the estimated hospitalizations and deaths were in people younger than 65 years old. (9)

CLINICAL MANIFESTATIONS

The clinical manifestations of novel 2009 influenza are similar to seasonal influenza. The symptoms include abrupt onset of fever, cough, sore throat, myalgias, arthralgias, chills, headaches and fatigue. Gastrointestinal symptoms (vomiting and diarrhea) have been reported more commonly with the novel 2009 influenza than the seasonal influenza. Similar to seasonal flu, some patients may not present with fever. (10). Clinical manifestation can range from uncomplicated influenza, to primary viral pneumonia, to secondary bacterial pneumonia. (5) Viral pneumonia begins with the typical onset of influenza, but symptoms progress to dyspnea, cyanosis, chest pain, severe dehydration, altered mental status or exacerbations of underlying conditions. Secondary bacterial pneumonia produces a syndrome that has a classic influenza illness followed by a period of improvement, then a recrudescence of fever and signs and symptoms of bacterial pneumonia. The most common pathogens include *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Staphylococcus aureus*. Viral pneumonia and secondary bacterial pneumonia require medical treatment and hospitalization. (5)

DIAGNOSIS

There are multiple diagnostic tests available to detect influenza in respiratory specimens. These tests have different sensitivity and specificity for detecting influenza. Rapid influenza tests are widely available, but the sensitivity is variable. The CDC recommends using the real-time reverse transcriptase polymerase chain reaction (rRT-PCR) where available. It has high sensitivity and specificity for influenza. See Table 1 for details.

Patients with suspected or confirmed 2009 novel influenza who require hospitalization should be given priority for diagnostic testing and should receive immediate empiric therapy. It is important to identify hospitalized patients with influenza in order to improve clinical care and adhere to proper infection control. Treatment and infection control measures should not be delayed pending diagnostic testing. Patients with uncomplicated influenza and who live in an area with circulating 2009 novel influenza do not require diagnostic testing for clinical management. (11)

TREATMENT

The available antiviral medications target either the neuraminidase protein or the M2 protein. The neuraminidase inhibitors, oseltamivir and inhaled zanamivir, act by inhibiting the activity of neuraminidase. Neuraminidase cleaves the terminal sialic acid from the sialic acid glycoproteins that serve as host-cell receptors for attachment of the influenza viruses. The adamantanes, rimantidine and amantadine, inhibit the activity of the M2 ion channel. The M2 ion channel acidifies the interior of the virion, allowing for replication to occur. Unlike neuraminidase inhibitors, adamantanes are only active against influenza A, not influenza B and C. One of the unique properties of the 2009 novel influenza (H1N1) is that it is inherently resistant to adamantanes. (5,6,7,10)

Zanamivir is not absorbed orally, so it is only available as a dry powder inhalation formulation; whereas, oseltamivir is readily absorbed orally. After GI absorption, it is converted to its active metabolite by hepatic esterases to oseltamivir carboxylate. The metabolite is excreted unchanged in the urine. The most common side effects are nausea and vomiting which can be alleviated when taken with food. Dose adjustment should be made for patients with renal dysfunction. (5) Zanamivir is supplied in blister packs for inhalation using the diskhaler device (GlaxoSmithKline). Due to increased risk of bronchospasm, inhaled zanamivir is not recommended in individuals with underlying airway disease (e.g. asthma, COPD, etc). (10) The dry powder contains 20mg of lactose so patients with history of a serious allergic reaction to lactose should avoid zanamivir. There is limited systemic absorption of inhaled zanamivir; therefore, no dosage adjustment is required for patients with renal dysfunction. (5,10)

The efficacy of oseltamivir and zanamivir has not been formally studied in patients with novel 2009 influenza, but

these agents remain the drugs of choice by the CDC. (10) Oseltamivir has been studied in patients with uncomplicated influenza. When administered within the first 36 hours of symptom onset, there can be expected up to a 40% reduction in duration of symptoms and severity of illness with reduced rates of prolonged coughing. Early therapy also resulted in earlier resumption of normal activities. Similar results have been found with inhaled zanamivir in patients with uncomplicated influenza. (5)

Patients with mild or uncomplicated illness characterized by fever, cough, sore throat, rhinorrhea, muscle pain, headache, chills and malaise without shortness of breath or changes in chronic illness may not require treatment. The treatment may not be beneficial in patients if treatment is initiated after 48 hours of illness onset. Patients with co-morbid conditions that may increase likelihood of complications related to influenza should be treated and monitored closely. These patients include children less than 2 years old, adults greater than 65 years old, pregnant women (up to 2 weeks post-partum), and person with co-morbid conditions (see Table 2.). Thus the CDC recommends prompt empiric antiviral treatment. (10)

Pregnant women have an increased risk of complications, hospitalizations and severe disease with the 2009 novel influenza. Jamieson et al found that pregnant women with novel 2009 influenza are four times more likely to be hospitalized than the general population (12). Despite the neuraminidase inhibitors being a pregnancy category C (i.e. lack of clinical studies available to assess safety), the CDC recommends prompt antiviral therapy. Oseltamivir is recommended over inhaled zanamivir because of its systemic activity. (10)

Treatment is also recommended for patients with suspected or confirmed 2009 H1N1 influenza with severe, complicated or progressive illness or patients who are hospitalized. Despite the majority of data supporting treatment within 48 hours of illness onset, limited observational data suggests that patients with severe disease may reduce mortality and duration of hospitalization if treated after 48 hours of symptom onset. (13) Antiviral doses and durations are listed in Table 3. Some experts suggest doubling the approved dose of oseltamivir for severely ill patients, but there are no published data suggesting benefit over the approved dose. The FDA has authorized the emergency use of oseltamivir for infants less than 1 year old. This is outside of the approved indications. The FDA issued the EUA in response to the declaration of public health emergency. (10)

Inhaled zanamivir may also be used in the hospitalized population but should only be used with the provided diskhaler device. Zanamivir should not be given as aerosolized solution via nebulizer, ventilator or other devices or other methods not approved. For hospitalized patients unable to take oral medications, the CDC has authorized the use of peramivir. Peramivir is an investigational agent available from the CDC under emergency use authorization (EUA.) (10, 13) Emergency use authorization allows clinicians to use peramivir under specified conditions. Peramivir is the first EUA issued for an unapproved drug. The FDA has the authority to issue an EUA only after the secretary of health and human services has declared a public health emergency, and it is reasonable to believe that the product may be effective and there are no other adequate approved alternatives. (10)

Peramivir is an investigational neuraminidase inhibitor with limited safety and efficacy data available. There are four clinical trials completed evaluating the efficacy of peramivir. In patients with acute, uncomplicated seasonal influenza, there was improvement in symptoms one day sooner than placebo. Peramivir was compared to oseltamivir but no conclusions about efficacy could be made because a clinically significant margin of non-inferiority was not achieved. The last study compared different doses of peramivir. Peramivir was not studied in severely ill patients or pediatric patients. Because of the lack of alternative intravenous options the CDC established criteria for appropriate use. Peramivir may be clinically appropriate for patients not responding to either oral or inhaled antiviral therapy, drug delivery by a route other than IV is not feasible, or the clinician judges IV therapy is appropriate due to other circumstances. Although there is no clinical data in the pediatric populations, peramivir may be appropriate in patients not responding to current oral or inhaled therapy or if drug delivery by a route other than IV (e.g. enteral oseltamivir) is not expected to be feasible. The usual adult dose of peramivir is 600mg daily for 5 to 10 days. The dose should be adjusted for renal dysfunction. The most common side effects include diarrhea, nausea, vomiting and neutropenia. (10,14)

The distribution of intravenous peramivir was handled electronically by the CDC (www.cdc.gov/h1n1/eua/peramivir.htm). Because this is an unapproved drug, clinicians are required to submit all adverse events and deaths to the CDC. Unlike other unapproved drugs, approval by the local institutional review board (IRB) is not required. Patients and caregivers are required to be informed of other alternatives but are not required to sign an informed consent. (10, 14)

RESISTANCE

As of December 8th 2009, 109 cases of oseltamivir-resistant 2009 H1N1 virus had been detected and reported to the World Health Organization (15). A majority of the cases occurred while taking oseltamivir for treatment of the novel 2009 H1N1 virus. Approximately one-third of the cases occurred in patients who were immunosuppressed. Prevention strategies (vaccinations and infection control measures) are emphasized with these vulnerable patient populations and their caregivers. In Washington State, two immunocompromised patients developed oseltamivir resistance while on therapy. The virus strain was identified as having a mutation involving a substitution of histidine for tyrosine at position 275 of the neuraminidase gene (H275Y). Zanamivir remained active in these two patients with the H275Y mutation. (16)

VACCINATIONS

The single most effective method of preventing influenza associated morbidity and mortality is vaccination. Previous seasonal influenza vaccines did not appear to provide immunity against the novel 2009 H1N1 influenza virus; therefore, massive efforts were undertaken to manufacture and license an effective vaccine promptly. The process for the development of the novel 2009 H1N1 vaccine followed the same standards used for the development of the seasonal vaccine. The Food and Drug Administration (FDA) approved four inactivated vaccines and one live virus vaccine against the 2009 H1N1 influenza in mid-September of 2009, but they were not available for distribution until the end of October due to manufacturer barriers. (17, 18, 19)

Because of serious complications of influenza in certain populations and initial limited supplies of vaccines, the CDC's Advisory Committee on Immunization Practices (ACIP) set forth recommendations for administration in five target populations. These high risk population (in no specific order) were pregnant women, persons who live with or provide care for infants (< 6 months old), health-care and emergency medical services personnel, persons-aged 6 months to 24 years, and persons aged 25 to 64 with medical conditions placing them at higher risk for influenza-related complications. (17) The five target groups represented approximately 159 million people in the United States. The ACIP provided a subset of the initial five target populations to provide guidance should vaccine demands exceed the initial supply. The subset populations include pregnant women, persons who live with or provide care for infants (< 6 months of age), health care professionals with direct patient care, children aged 6 months to 4 years and children and adolescents aged 5 to 18 years with co-morbid conditions. See Table 4 for specific details. Chronic medical conditions that pose a higher risk for influenza-related complications include chronic pulmonary conditions (including asthma), cardiovascular (except hypertension), renal, hepatic, cognitive, neurologic/neuromuscular, hematologic, or metabolic disorders (including diabetes mellitus) or immunosuppression (including immunosuppression caused by medications or by human immunodeficiency virus). At this time, the needs of the target populations are met, so the influenza vaccine should be given to all populations. (17, 18, 19)

The vaccine is currently available as a live-attenuated (nasal spray) and inactivated (injection) formulations. The inactivated vaccine is available from multiple manufacturers. The FDA-approved route of administration for the live-attenuated is the intra-muscular route. In adults and older children, it should be administered in the deltoid muscle using a 1 inch needle. In infants and young children, the vaccine should be administered in the anterolateral aspect of the thigh. The inactivated vaccines in multi-dose vials contain the preservative thimersol, but single-dose preparations are available without vaccine preservatives. A single administration of the novel 2009 H1N1 vaccine resulted in a robust response in adults > 18 years of age, therefore requiring only one dose. Children less than 10 years of age required 2 vaccinations separated by at least 21 days. See Table 5. (6,17,18)

The same vaccine is available as a live-attenuated influenza vaccine (LAIV) for intranasal administration. The LAIV is approved for use in patients from 2 to 49 years of age who are NOT pregnant and do not exhibit certain health conditions (e.g. immunocompromised, anyone with long-term health conditions, etc). Because it is a live vaccine, it is shipped in a refrigerated container and should be stored in the pharmacy between 36F to 46F degrees. It is available in a pre-filled single sprayer containing 0.2ml of vaccine. Half of the contents should be sprayed (approximately 0.1mL) into the one nostril and repeated into the other nostril. LAIV should not be administered to patients with asthma, as they may be at increased risk for wheezing. LAIV is contraindicated in patients with hypersensitivity to eggs, egg protein, gentamicin, gelatin, or arginine or life-threatening reactions to previous influenza vaccination. LAIV does not cause influenza but in some patients, it can cause temporary nasal congestion or fever. The dose and schedule is provided in Table 5. (19) The LAIV novel 2009 influenza vaccine should not be co-administered with the seasonal LAIV.

According to CDC estimates as of January 2, 2010, 20.3% of the US population, approximately 61 million people, had been vaccinated. It is approximated that 27.9% of the initial target population were vaccinated and 37.5% of the subset population were vaccinated. (17) The vaccine is available for the general population, and the CDC is encouraging all populations to become vaccinated. (17, 19)

INFECTION CONTROL/VACCINATION POLICIES

Infection control measures are necessary to prevent transmission within a healthcare setting among patients, caregivers and healthcare personnel. The CDC has developed guidelines for appropriate infection control measures for healthcare facilities and personnel. (8) In order of importance, the following practices are recommended by the CDC: elimination of potential exposures (e.g. denying entry to visitors who are sick), engineering controls (e.g. installing partition barriers in triage areas), administrative controls (e.g. employee vaccination programs), and providing protective equipment (PPE). It is important to emphasize the importance of the first three measures to avoid reliance on PPE, due to shortage of respirator supplies. In order to protect healthcare workers and their patients, some institutions have mandated all employees receive influenza vaccinations to improve vaccination rates. A large-Midwestern health care organization required vaccination for all healthcare employees to enhance vaccination rates. Healthcare workers were terminated if they did not have a religious or medical exemption. Mandatory employee vaccinations successfully improved vaccination rates from 71% to 98% after the policy was implemented. (20)

In addition to infection control measures in the healthcare settings, patients should be educated about preventative measures including use of good respiratory hygiene, frequent hand washing, alcohol based hand gel, avoiding contact with ill-persons and staying home from work when ill. (8)

PHARMACY PERSPECTIVES

Pharmacists were a vital component of the control and management of the novel 2009 influenza outbreak by administering vaccinations, distributing antivirals and providing patient education. In many states, pharmacists are permitted to administer vaccinations without a prescription. (21) The American Pharmacists Association has estimated that pharmacists have received 5.4 million total doses of H1N1 vaccine. (22)

The pandemic 2009 influenza has affected pharmacists because greater numbers of patients seek to fill prescriptions for influenza, antibiotics to treat secondary infections and seek advice regarding over the counter cough and cold medications and vaccinations. Antiviral availability from the manufacturers and distributors are steady, but shortages have been reported with the commercially manufactured Tamiflu[®] suspension. The CDC has provided recommendations for the appropriate compounding of oseltamivir suspension from the capsules. Unfortunately, the commercially available Tamiflu[®] suspension (available as 12 mg/ml) and the compounded oseltamivir (15mg/ml) have different concentrations which may lead to dosing errors. Prescribers must specify the dose in mg, rather than mls to avoid possible dosing errors. (23,24)

SUMMARY AND FUTURE CONSIDERATIONS

As of February 28th, 2010, the WHO estimated more than 213 countries had reported laboratory confirmed cases of novel 2009 influenza (H1N1), which included at least 16,455 deaths. In the northern hemisphere, transmission continues but at low levels. The most active areas include Southeast Asia and East and South-eastern Europe. (25)

The novel 2009 influenza (H1N1) has created the first influenza pandemic in 40 years. Unlike previous epidemics, some of the population has had previous exposure. In contrast to previous seasonal influenza epidemics, the younger populations are disproportionately affected. It is unknown whether H1N1 will displace, co-circulate or mutate with the seasonal influenza virus. It is essential for clinicians, including pharmacists, to remain updated on the novel 2009 influenza pandemic as the situation develops and evolves.

Table 1. Available diagnostic tests for the novel 2009 influenza virus

Diagnostic test	Detection Method	Typical processing time	Sensitivity for 2009 H1N1 influenza	Comments
Rapid influenza diagnostic tests	Antigen	0.5 hour	10-70%	Widely available; Does not distinguish between 2009 H1N1 and other influenza
Direct and indirect immunofluorescence assays (DFA and IFA)	Antigen	2- 4 hours	47-93%	Widely available; Does not distinguish between 2009 H1N1 and other influenza
Viral isolation in tissue cell culture	Virus	2- 10 days		Limited availability; Distinguishes between 2009 H1N1 from other influenza
Nucleic acid amplification tests	RNA detection	48- 96 hours	86-100%	Limited availability; Distinguishes between 2009 H1N1 from other influenza

Adapted from Reference 11.

Table 2. Conditions associated with increased risk of complications of influenza

Children < 2 years old
Adults ≥ 65 years old
Pregnant women
Immunosuppressed patients (AIDS, cancer or those on chronic steroids)
Chronic medical conditions:
Asthma
Neurological and neuro-developmental conditions
Chronic lung diseases
Heart disease (congenital heart disease, coronary artery disease, congestive heart failure, not hypertension)
Hematologic diseases (sickle cell disease)
Endocrine disorders (diabetes mellitus)
Renal or hepatic disorders
Chronic aspirin use in patients less than 19 years of age

Adapted from References 17,18,19

Table 3. Recommended doses for Antiviral therapy for treatment and prophylaxis for the novel 2009 influenza (H1N1)

Medication	Treatment Dose	Chemoprophylaxis	Comments
Oseltamivir	(5 days)	(10 days)	
Adults			
	75mg twice daily	75mg once daily	
Children ≥ 12 months			
Body Weight			
≤ 15 kg	30mg twice daily	30mg once daily	
>15 kg to 23 kg	45mg twice daily	45mg once daily	
23 kg to 40kg	60mg twice daily	60mg once daily	
>40kg	75mg twice daily	75mg once daily	
Children < 11 months			
6-11 months	25mg twice daily	25mg once daily	Authorized by the FDA EUA
3-5 months	20mg twice daily	20mg once daily	
< 3 months	12mg twice daily	Not recommended	

Zanamivir			
Adults			
	10mg (2 x 5mg inhalations) twice daily	10mg (2 x 5mg inhalations) once daily	
Children	10mg (2 x 5mg inhalations) twice daily in children \geq 7 years old	10mg (2 x 5mg inhalations) once daily in children > 5 years old	

Adapted from References 10

Table 4. Target Populations for 2009 novel influenza vaccine

Initial Target population	Subset population if supplies diminish
Pregnant women	Pregnant women,
Persons who live with or provide care for infants aged < 6 months	Persons who live with or provide care for infants aged <6 months (e.g., parents, siblings, and daycare providers),
Healthcare personnel and emergency medical services	Healthcare and emergency medical services personnel who have direct contact with patients or infectious material,
Persons aged 6 months to 24 years old	Children aged 6 months—4 years, and
Persons aged 25 to 64 years with medical conditions predisposing them to influenza-related complications	Children and adolescents aged 5—18 years who have medical conditions that put them at higher risk for influenza-related complications.

Adapted from Reference 17, 18,19

Table 5. Available novel 2009 influenza (H1N1) vaccines

Vaccine type / Route	Manufacturer	Available Formulation	Mercury content (g Hg/0.5 ml dose)	Age group	No. of doses	Comments
Inactivated/ IM	<u>Sanofi Pasteur</u>	0.25 ml prefilled syringe	0	6–35 months	2	2 doses separated by 4 weeks (>21 days)
		0.5 ml prefilled syringe	0	≥36 months to 9 years	2	2 doses separated by 4 weeks (>21 days)
				≥10 years	1	
		5.0 ml multidose vial	25.0	≥6 months	1 or 2	2 doses separated by 4 weeks (>21 days)
Inactivated/IM	<u>Novartis Vaccines and Diagnostics Limited</u>	5.0 ml multidose vial	25.0	≥4 yrs to 9 yrs	2	2 doses separated by 4 weeks (>21 days)
				≥10 yrs	1	
		0.5 ml prefilled syringe	<1.0	≥4 yrs	1 or 2	2 doses separated by 4 weeks (>21 days)
Inactivated/IM	<u>CSL Limited</u>	0.25 ml prefilled syringe	0	6–35 months	2	2 doses separated by 4 weeks (>21 days)
		0.5 ml prefilled syringe		≥3 yrs	1	
Inactivated/IM	<u>ID Biomedical</u> (Distributed by GSK)	5.0 ml multidose	25.0	≥18 yrs	1	
LAIV/Nasal	<u>MedImmune LLC</u>	0.2 ml sprayer	0	2– 9 yrs	2	2 doses separated by 4 weeks (>21 days)
LAIV/Nasal	<u>MedImmune LLC</u>	0.2 ml sprayer	0	>10–49 yrs	1	

Adapted from Reference 17, 18,19

REFERENCES

1. Centers for Disease Control and Prevention (CDC). Swine Influenza A (H1N1) Infection in Two Children—Southern California, March–April 2009 *Morb and Mortal Wkly Rep.* 2009; 58 (15): 400- 402.
2. Centers for Disease Control and Prevention (CDC). Update: Swine Influenza A (H1N1) Infections—California and Texas, April 2009 *Morb and Mortal Wkly Rep.* 2009. 58 (16): 435-7
3. Centers for Disease Control and Prevention (CDC). Novel H1N1 Flu: Background on the Situation. CDC website: <http://www.cdc.gov/H1N1FLU/background.htm>. Accessed March 7, 2010
4. World Health Organization. World now at the start of 2009 influenza pandemic. WHO website. http://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/print.html. Accessed March 7, 2010.
5. Treanor JJ. Influenza virus. In: Mandell GL, Bennett JE, Dolin R, eds. *Mandell, Douglas, and Bennett's Principles of and Practice of Infectious Diseases*. 7th ed. Philadelphia, PA. Elsevier Churchill Livingstone; online version.
6. Sullivan SJ, Jacobson RM, Dowdle WR, et al. 2009 H1N1 influenza. *Mayo Clin Proc.* 2010; 85(1): 64-76
7. Cunha BA. Swine Influenza (H1N1) Pneumonia: Clinical Considerations. *Infect Dis Clin N Am* 24 (2010) 203–228
8. Centers for Disease Control and Prevention (CDC). Interim Guidance on Infection Control Measures for 2009 H1N1 Influenza in Healthcare Settings, Including Protection of Healthcare Personnel. CDC website. http://www.cdc.gov/h1n1flu/guidelines_infection_control.htm. Accessed March 7, 2010.
9. Centers for Disease Control and Prevention (CDC). CDC Estimates of 2009 H1N1 Influenza Cases, Hospitalizations and Deaths in the United States, April 2009 – January 16, 2010 CDC website. http://www.cdc.gov/h1n1flu/estimates_2009_h1n1.htm. Accessed March 7, 2010.
10. Centers for Disease Control and Prevention (CDC). 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>. Accessed March 7th, 2010.
11. Centers for Disease Control and Prevention (CDC). Interim Recommendations for Clinical Use of Influenza Diagnostic Tests During the 2009-10 Influenza Season. http://www.cdc.gov/h1n1flu/guidance/diagnostic_tests.htm. Accessed March 7th, 2010.
12. Jamieson DJ, Honein MA, Rasmussen SA, et al. H1N1 2009 influenza virus infection during pregnancy in the USA. *Lancet.* 2009;374:451-458.
13. Uyeki T. Antiviral Treatment for Patients Hospitalized with 2009 Pandemic Influenza A (H1N1) *N Engl J Med.* 2009; 361: e110
14. Birnkrant D, Cox E. The Emergency Use Authorization of Peramivir for Treatment of 2009 H1N1 Influenza. *N Engl J Med* 2009; 361:2204.
15. World Health Organization. Pandemic (H1N1) 2009: antiviral drug resistance. http://www.who.int/csr/disease/swineflu/frequently_asked_questions/antivirals/resistance/en/. Accessed March 7, 2010.
16. Centers for Disease Control and Prevention (CDC). Oseltamivir-Resistant Novel Influenza A (H1N1) Virus Infection in Two Immunosuppressed Patients --- Seattle, Washington, 2009 *Morb and Mortal Wkly Rep.* 2009; 58(32);893-896
17. Centers for Disease Control and Prevention (CDC). Interim Results: Influenza A (H1N1) 2009 Monovalent Vaccination Coverage --- United States, October--December 2009 *Morb and Mortal Wkly Rep.* 2010; 59(02);44-48
18. Centers for Disease Control and Prevention (CDC). Use of Influenza A (H1N1) 2009 Monovalent Vaccine Recommendations of the Advisory Committee on Immunization Practices. *Morb and Mortal Wkly Rep.* 2009; 58;1-8
19. Centers for Disease Control and Prevention.(CDC). 2009 H1N1 Monovalent Influenza Vaccine Dosage, Administration, and Storage. <http://www.cdc.gov/h1n1flu/vaccination/dosage.htm>. Accessed March 7, 2010.
20. Babcock HM, Gemeinhar N, Jones M, et al. Mandatory Influenza Vaccination of Health Care Workers: Translating Policy to Practice. *Clin Infect Dis.* 2010; 50: 459-64.
21. American Society of Health System Pharmacists Council on Professional Affairs. ASHP Guidelines on Pharmacist's Role in Immunization. *Am J Health Syst Pharm.* 2003 Jul 1;60(13):1371-7
22. American Pharmacists Association. ACIP discusses broad range of vaccination topics. http://www.pharmacist.com/AM/Template.cfm?Section=Pharmacist_Immunization_Center1&CONTENTID=22481&TEMPLATE=/CM/HTMLDisplay.cfm. Accessed March 7, 2010.
23. Institute for Safe Medication Practice(ISMP). <http://www.ismp.org/safetyalerts/20091015-Tamiflu.asp>. ISMP website. Accessed March 7, 2010.
24. Centers for Disease Control and Prevention. (CDC). 2009 H1N1 Influenza: Resources for Pharmacists. CDC website. <http://www.cdc.gov/H1N1flu/pharmacist>. Accessed March 7, 2010.
25. World Health Organization. Pandemic (H1N1) 2009 – update 90. WHO website. http://www.who.int/csr/don/2010_03_05/en/index.html. Accessed March 7, 2010

Fill in the information below, answer questions and return **Quiz Only** for certification of participation to:
 CE PRN[®], 400 Lake Cook Road, Suite 207, Deerfield, IL 60015.

NAME _____ (ID # 1st line on label) _____

ADDRESS _____ CITY _____ STATE _____ ZIP _____

CHECK IF NEW ADDRESS **ARE YOU LICENSED IN FLORIDA? IF YES FL LIC** _____

EMAIL Address (we need this) _____

LESSON EVALUATION

Please fill out this section as a means of evaluating this lesson. The information will aid us in improving future efforts. Either circle the appropriate evaluation answer, or rate the item from 1 to 7 (1 is the lowest rating; 7 is the highest).

1. Does the program meet the learning objectives?

Describe epidemiology, diagnosis & basic virology associated with the 2009 H1N1 epidemic Yes No

List treatment options for the 2009 H1N1 virus Yes No

Discuss prevention strategies & vaccination recommendations for different age groups Yes No

2. Was the program independent & non-commercial Yes No

	Poor		Average		Excellent
	1	2	3	4	5

3. Relevance of topic 1 2 3 4 5 6 7

4. What did you like most about this lesson? _____

5. What did you like least about this lesson? _____

Please Select the Most Correct Answer

- | | |
|--|--|
| <p>1. Influenza is NOT transmitted via:
 A. Contact exposure
 B. Droplet exposure
 C. Oral & fecal exposure
 D. Airborne exposure</p> <p>2. The clinical manifestations of the novel 2009 influenza includes which of these?
 A. Viral meningitis
 B. Viral pneumonia
 C. Secondary bacterial pneumonia
 D. B & C</p> <p>3. Which of these are appropriate indications for the use of peramivir?
 A. Patients with seasonal influenza who CAN take PO antivirals
 B. Patients with novel 2009 influenza UNABLE to tolerate PO antivirals
 C. Patients with uncomplicated novel 2009 influenza
 D. A & C</p> <p>4. Pharmacists should be aware of dosing errors with the following medications:
 A. Peramivir
 B. Nebulized Zanamivir
 C. Oseltamivir suspension
 D. A & B</p> <p>5. The CDC recommends awaiting results of diagnostic testing prior to administering antiviral therapy for patients with suspected viral pneumonia.
 A. True B. False</p> | <p>6. Adamantanes are effective treatment for the novel 2009 influenza.
 A. True B. False</p> <p>7. Which of these groups are at high risk for influenza related complications?
 A. Adults > 65 years of age
 B. Pregnant women
 C. Patients with chronic conditions
 D. Immunosuppressed patients
 E. All of these</p> <p>8. Which groups require an additional dose of the novel 2009 influenza (H1N1)?
 A. Adolescents
 B. Adults > 65 years of age
 C. Adults with chronic conditions
 D. Children > 9 years of age
 E. Children < 10 years of age</p> <p>9. In comparison to seasonal influenza, the novel 2009 influenza has disproportionately affected which group?
 A. Adults < 65 years of age
 B. Adults > 65 years of age
 C. Children < 6 months of age
 D. Immunosuppressed patients</p> <p>10. Which antiviral has retained activity against the reported oseltamivir resistant strains?
 A. Peramivir
 B. Zanamivir
 C. Rimantidine
 D. All of these
 E. None of these</p> |
|--|--|

Contributing Author

Rupali Jain, PharmD, BCPS, AAHIVE
Clinical Assistant Professor
Antimicrobial Stewardship
University of Washington, School of Pharmacy
Seattle, WA

**CORRECT
FAX
847-945-5037**

Executive Editor

William J. Feinberg,
BS Pharm, MBA



CE PRN[®] is a publication of W-F Professional Associates, Inc. This program is in printed format.

W-F Professional Associates, Inc. is approved by the Accreditation Council for Pharmaceutical Education (ACPE) as a provider of continuing pharmaceutical education.

Providers who are approved by ACPE are recognized by the following states: Alaska, Arizona, Arkansas, California, Colorado, Connecticut, Delaware, District of Columbia, Florida, Georgia, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oregon, Pennsylvania, Puerto Rico, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin and Wyoming.

Pharmacists completing this course by June 30, 2013 may receive full credit.

This lesson furnishes 1.25 hours (0.125 CEUs) of credit.

Program ID #707-000-10-006-H01-P.

CE Provider Registered # with CE Broker.com is 50-3170.