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REVIEW

Treatment and Prevention of Pandemic H1N1 Influenza

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Abstract

BACKGROUND Swine influenza is a respiratory infection common to pigs worldwide caused by type A influenza viruses, principally subtypes H1N1, H1N2, H2N1, H3N1, H3N2, and H2N3. Swine influenza viruses also can cause moderate to severe illness in humans and affect persons of all age groups. People in close contact with swine are at especially high risk. Until recently, epidemiological study of influenza was limited to resource-rich countries. The World Health Organization declared an H1N1 pandemic on June 11, 2009, after more than 70 countries reported 30,000 cases of H1N1 infection. In 2015, incidence of swine influenza increased substantially to reach a 5-year high. In India in 2015, 10,000 cases of swine influenza were reported with 774 deaths.

METHODS The Centers for Disease Control and Prevention recommend real-time polymerase chain reaction as the method of choice for diagnosing H1N1. Antiviral drugs are the mainstay of clinical treatment of swine influenza and can make the illness milder and enable the patient to feel better faster.

FINDINGS Antiviral drugs are most effective when they are started within the first 48 hours after the clinical signs begin, although they also may be used in severe or high-risk cases first seen after this time. The Centers for Disease Control and Prevention recommends use of oseltamivir (Tamiflu, Genentech) or zanamivir (Relenza, GlaxoSmithKline).

CONCLUSION Prevention of swine influenza has 3 components: prevention in swine, prevention of transmission to humans, and prevention of its spread among humans. Because of limited treatment options, high risk for secondary infection, and frequent need for intensive care of individuals with H1N1 pneumonia, environmental control, including vaccination of high-risk populations and public education are critical to control of swine influenza out breaks.

KEYWORDS clinical features, diagnosis, epidemiology, H1N1 influenza, treatment

INTRODUCTION

Global pandemics with high mortality and morbidity occur when a virulent new viral strain emerges, against which the human population has no immunity.[1] The influenza A virus was responsible for 3 global pandemics in the past century: Spanish flu in 1918, Asian flu in 1957, and Hong Kong flu in 1968.[2-4] Influenza virus outbreaks occur with regularity, but their severity varies.

Swine Influenza is a respiratory disease common among pigs caused by type A influenza, principally subtypes H1N1, H1N2, H2N1, H3N1, H3N2, and H2N3.[5,6] The influenza virus belongs to the

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Annals of Global Health, VOL. 81, NO. 5, 2015
September–October 2015: 645–653

genus *Orthomyxovirus* in the family *Orthomyxoviridae*, which consists of influenza A, B, and C viruses[7] and has an envelope, is single-stranded, negatively sensed RNA, 8 separate segments, and pleomorphic appearance with an average diameter of 120 nm.[7-10]

EPIDEMIOLOGY

The novel H1N1 strain, which is responsible for the current global pandemic of swine origin influenza, was first recognized at the border between Mexico and United States in April 2009. During a short span of 2 months, it became the first pandemic of the 21st century.[11] Before this time, the same triple reassorted virus was isolated in swine as early as 1998 with sporadic infections in humans as well.[12,13] The pandemic influenza A H1N1 2009 virus (A/2009/H1N1) caused the first pandemic influenza of the new millennium, and has affected more than 214 countries and caused more than 18,449 deaths.[14]

It is estimated that the influenza pandemic that started with the 1918 Spanish flu killed 20 to 50 million people worldwide, followed by epidemics of Asian flu in 1957, Hong Kong flu in 1968, and Russian flu in 1977, each with random and severe attacks on human populations.[1] The H1N1 form of swine flu is a descendent of the strain that caused the 1918 flu pandemic. As well as persisting in pigs, the descendants of the 1918 virus also circulated in humans throughout the 20th century, contributing to the normal seasonal epidemics of influenza.[15]

The first identification of an influenza virus as a cause of disease in pigs occurred in 1930. For the next 60 years, swine influenza strains were almost exclusively H1N1. Then, between 1997 and 2002, new strains of 3 different subtypes and 5 different genotypes emerged as causes of influenza among pigs in North America.[12] On August 13, 2009, the World Health Organization reported that 1,82,166 laboratories confirmed cases of influenza A/H1N1, with 1799 deaths in 178 countries. In 2015, the incidence of swine flu increased substantially to reach 5-year highs with more than 10,000 cases and 774 deaths reported.

CLINICAL FEATURES

Important clinical features of swine influenza include fever and upper respiratory symptoms such as cough, runny nose, and sore throat. Headache, body aches, fatigue, diarrhea, and vomiting also have been observed.[2] There is insufficient information to date about clinical complications of the current pandemic influenza A (H1N1) virus infection. Clinicians should expect complications to be similar to seasonal influenza: sinusitis, otitis media, croup, pneumonia, bronchiolitis, status asthmaticus, myocarditis, pericarditis, myositis, rhabdomyolysis, encephalitis, seizures, toxic shock syndrome, and secondary bacterial pneumonia with or without sepsis.[2,16] Individuals at extremes of age and with pre-existing medical conditions are at higher risk for complications and exacerbation of the underlying conditions.[16,17]

DIAGNOSTIC TESTS

Routine investigations required for evaluation and management of a patient with the symptoms just described are required. These may include hematological, biochemical, radiological, and microbiological tests as necessary. A diagnosis of confirmed swine flu requires laboratory testing of a respiratory sample (a simple nose and throat swab). Tests used to detect influenza virus infections in humans can include reverse transcriptase polymerase chain reaction (RT-PCR), virus isolation, and assays to detect a 4-fold rise detect influenza virus antigens.[18-21] Many recent swine influenza cases were diagnosed by genetic methods, particularly RT-PCR.[22]

Routine diagnostic tests used to detect human influenza viruses, including commercial rapid test kits, do not necessarily detect zoonotic viruses.[19,20,23-25] One indication that a novel, possibly zoonotic influenza, virus might be present is the detection of influenza A virus, but not the hemagglutinins in seasonal human influenza viruses.[19] Zoonotic influenza virus infections are occasionally diagnosed retrospectively by serology,[26,27] but serological diagnosis can be complicated by cross-reactivity with human influenza viruses. A further difficulty is that the hemagglutinin (HA) and neuraminidase (NA) of some swine influenza viruses (the main targets of antibody responses) originally came from human influenza viruses, to which people may have already been exposed. State, regional, or national public health laboratories generally test for novel influenza viruses.[19,21]

Real-time RT-PCR. The Centers for Disease Control and Prevention (CDC) has developed an rRT-PCR assay to detect seasonal influenza A, B, H1, H3, and avian H5 serotypes. This assay has been approved by the Food and Drug Administration and was distributed in December 2008 through US public health laboratories and the World Health Organization's Global Influenza Surveillance Network. The CDC's rRTPCR Protocol for Detection and

Characterization of Swine Influenza includes a panel of oligonucleotide primers and dual-labeled hydrolysis (Taqman) probes to be used in rRT-PCR assays for the in vitro qualitative detec- tion and characterization of swine influenza viruses in respiratory specimens and viral cultures. The InfA primer and probe set is designed for universal detection of type A influenza viruses. The swInfA primer and probe set is designed to specifically detect all swine influenza A viruses. The swH1 primer and probe set is designed to specifically detect swine H1 influenza. This assay is used for testing influenza A-positive respiratory specimens (unsubtypable) taken from suspect swine influenza A-infected patients.[28-30]

Nucleotide Sequencing and Phylogenetic Analysis. Amplicons for gene sequencing were generated by reverse transcription, followed by PCR amplification to generate overlapping double-stranded DNA amplicons covering each of 8 segments of the influenza virus genome.

Phylogenetic Analysis. Phylogenetic analysis of sequences contained 6 gene segments (PB2, PB1, PA, HA, NP, and NS) that were found in triple-reassortant swine influenza viruses circulating in pigs. The genes encoding neuraminidase and M protein were most closely related to those in influenza A viruses circulating in swine populations.[28]

For confirmation of diagnosis, clinical specimens such as nasopharyngeal swab, throat swab, nasal swab, wash or aspirate, and tracheal aspirate (for intubated patients) are to be obtained. The sample should be collected by a trained physician or microbiologist preferably before administration of the antiviral drug. Specimens should be kept at 4°C in viral transport media until transported for testing. The samples should be transported to designated laboratories with in 24 hours. If they cannot be transported then they MUST be stored at −70°C. Paired blood samples at an interval of 14 days for serological testing should also be collected.[31,32]

TREATMENT

The guiding principles of treatment are as follows:

- Early implementation of infection control precautions to minimize household spread of disease.
- Prompt treatment to prevent severe illness and death.
- Early identification and follow-up of individuals at risk.

The following infrastructure, manpower, and material support are needed:

- Isolation facilities: If a dedicated isolation room is not available, patients can be cohorted in a well-ventilated isolation ward with beds kept 1 m apart.
- Manpower: dedicated doctors, nurses, and paramedics.
- Equipment: portable x-ray machine, ventilators, large oxygen cylinders, pulse oximeter.
- Supplies: adequate quantities of personal protective equipment (PPE), disinfectants, and medications (oseltamivir, antibiotics, and other medicines).[3]

Standard operating procedures include the following:

- Standard infection control precautions should be reinforced (ie, all those entering the room must use high-efficiency masks, gowns, goggles, gloves, caps, and shoe covers).
- The number of visitors must be restricted and they must be provided with PPE.
- Antiviral prophylaxis must be provided to health care personnel managing the case and they should be asked to monitor their own health twice a day.
- Waste must be disposed properly by being placed in sealed impermeable bags labeled as bio-hazard.[3]

Medication. Two groups of antiviral drugsdthe adamantanes (amantadine, rimantadine), and neuraminidase inhibitors (zanamivir, oseltamivir, peramivir, and laninamivir)dare used to treat some cases of influenza, although some of these drugs (peramivir and laninamivir) are not licensed in all countries.[33-37] Both groups of drugs are effective against some influenza A viruses, although they may have some side effects. Antiviral drugs are most effective if they are started within the first 48 hours after the clinical signs begin, although they also may be used in severe or high-risk cases first seen after this time.[33,35] Antiviral resistance can develop rapidly and may emerge during treatment.[33,34,38,39] One recent study reported resistance to neuraminidase inhibitors in 9% of swine influenza viruses that contained the N2 neuraminidase (H1N2, H3N2, and H9N2).[39]

Zanamivir and oseltamivir are members of a new class of drugs called neuraminidase inhibitors and are active against both influenza types A and B. Zanamivir is provided as a dry powder that is administered by inhalation. It is approved for treatment of uncomplicated acute influenza A or B in patients aged 7 years and older who have been symptomatic for less than 48 hours. Oseltamivir is provided as an oral capsule. It is approved for the treatment of uncomplicated influenza A or B in individuals at least 1 year of age who have been symptomatic for less than 48 hours. Zanamivir is approved for prophylaxis

Annals of Global Health, VOL. 81, NO. 5, 2015
September–October 2015: 645–653

of influenza in patients 5 years and older. Oseltamivir is approved for prophylaxis of influenza infection in individuals no younger than 1 year of age.[39]

In 2007–2008, a significant increase in the prevalence of oseltamivir resistance was reported among influenza A (H1N1) viruses worldwide. During the 2007–2008 influenza seasons, 10.9% of H1N1 viruses tested in the United States were resistant to oseltamivir. During 2008, more than 90% of H1N1 viruses were resistant to oseltamivir. During the 2008–2009 influenza seasons, the CDC recommended that individuals who tested positive for influenza A receive only zanamivir if treatment was indicated. Oseltamivir should be used alone only if recent local surveillance data indicate that circulating viruses are likely to be influenza A (H3N2) or influenza B viruses, which have not been found to be resistant to oseltamivir.[40]

Antiviral agents for influenza are an adjunct to vaccine and are not a substitute for vaccine. Vaccination remains the principal means for preventing influenza-related morbidity and mortality.[41] Presently, the government of India recommends Tamiflu as a drug of choice. Tamiflu is available at all government health offices. Human influenza A is susceptible to both oseltamivir and zanamivir, 2 antiviral medications approved for the prevention and treatment of influenza in the United States.[42]

Oseltamivir is the recommended drug both for prophylaxis and treatment (see Table 1 for dosing). In the current phase, if a person conforms to the case definition of suspect case, he or she would be provided oseltamivir.[40,43] Oseltamivir is generally well tolerated. Gastrointestinal side effects (nausea, vomiting) may increase with increasing doses, particularly those above 300 mg per day. Occasionally, side effects may include bronchitis, insomnia, and vertigo. Less commonly, angina, pseudomembranous colitis, and peritonsillar abscess have been reported. There have been rare reports of anaphylaxis and skin rashes.[43]

Table 1. Oseltamivir Dosing

By Weight	For Infants (By Age)*
▫ For weight <15 kg: 30 mg bid for 5 d	▫ <3 mo: 12 mg bid for 5 d
▫ 15–23 kg: 45 mg bid for 5 d	▫ 3–5 mo: 20 mg bid for 5 d
▫ 24 to <40 kg: 60 mg bid for 5 d	▫ 6–11 mo: 25 mg bid for 5 d
▫ >40 kg: 75 mg bid for 5 d	

* Also available as syrup (12 mg/mL).

SUPPORTIVE THERAPY

Supportive care for uncomplicated influenza in humans includes administration of fluids and rest. Additional adjunctive and supportive treatments for more severe cases vary and can include various drugs, including antibiotics to treat or prevent secondary bacterial pneumonia, intravenous fluids, parenteral nutrition, oxygen therapy or ventilatory support, and vasopressors for shock.[44]

Paracetamol or ibuprofen can be prescribed for fever, myalgia, and headache. Patients are advised to drink plenty of fluids. Smokers should avoid smoking. Salicylates, or aspirin, are strictly contraindicated in any influenza patient because of their potential to cause Reye's syndrome. Patients with signs of tachypnea, dyspnea, respiratory distress, and oxygen saturation less than 90% should be supplemented with oxygen therapy. Patients with severe pneumonia and acute respiratory failure (blood oxygen <90% and partial pressure of oxygen <60 mm Hg with oxygen therapy) must be supported with mechanical ventilation.[45]

Airway, breathing, and circulation must be maintained, as should hydration, electrolyte balance, and nutrition. If laboratory reports are negative, the patient should be discharged after receiving a full course of oseltamivir. Immunomodulating drugs have not been found beneficial in treatment of acute respiratory distress syndrome or sepsis-associated multiorgan failure. High-dose corticosteroids in particular have no evidence of benefit and there is potential for harm. Low-dose corticosteroids (hydrocortisone 200–400 mg/d) may be useful in persisting septic shock (systolic blood pressure <90). Suspected cases not having pneumonia do not require antibiotic therapy. Antibacterial agents should be administered, if required, as per locally accepted clinical practice guidelines. Patients on mechanical ventilation should be given antibiotics prophylactically to prevent hospital-associated infections.[45]

DISCHARGE POLICY

It has been observed that some patients, despite being asymptomatic, continue to test positive for influenza A H1N1. A patient who has been treated and has recovered, despitetesting positive, has very little possibility of infecting others. In view of this, the following recommendations have been made[46]:

- Patients who responded to treatment after 2 or 3 days and who become totally asymptomatic should be discharged after 5 days of treatment. There is no need for a repeat test.

- Patients who continue to have symptoms of fever, sore throat, etc., even on day 5, should continue treatment for an additional 5 days. If these patients become asymptomatic during the course of treatment, there is no need to test further.
- For patients who continue to be symptomatic even after 10 days of treatment or for those individuals with respiratory distress and in whom secondary infection is taken care of, and if patients continue to shed virus, then these individuals should be tested for resistance to antiviral. The dose of antiviral may be adjusted on case-by-case basis. The family of patients discharged earlier should be educated about personal hygiene and infection control measures at home; children should not attend school during this period.[46]

CHEMOPROPHYLAXIS

The treating physicians and other paramedical personnel at the isolation facility are considered at high risk and should be put on chemoprophylaxis.[47] Chemoprophylaxis is advised for those contacts at high risk (ie, those with underlying systemic diseases; those younger than 5 years; and those 65 years or older). In phase 5, if the clusters are reported for the first time, and given that those exposed are known and can be traced easily, then family, social, and community contacts should be given chemoprophylaxis.[47]

Mass Chemoprophylaxis. The strategy of containment by geography, an approach that includes giving oseltamivir to every individual in a prescribed geographic limit of 5 km from the epicenter, would be applied for the following reasons:

- If the virus is lethal and causing severe morbidity and high mortality.
- Although affecting humans, the virus is not efficiently transmitting in the population.
- If the cluster is limited by natural geographic boundaries.
- All close contacts of suspected, probable, and confirmed cases. Close contacts include household and social contacts, family members, workplace or school contacts, fellow travelers, and so on.
- All health care personnel coming in contact with suspected, probable, or confirmed cases.

Oseltamivir is the drug of choice and prophylaxis should be provided until 10 days after the individual's last exposure (maximum period of 6 weeks).

NONPHARMACEUTICAL INTERVENTIONS

Close contacts of suspected, probable, and confirmed cases should be advised to remain at home for at least 7 days after the last contact with the case. Monitoring of fever should be done for at least 7 days. Prompt testing and hospitalization are required when symptoms are reported. All suspected cases and clusters of influenza-like illness or severe acute respiratory infection cases need to be reported to the state health authorities and the Ministry of Health and Family Welfare, Government of India (director, Emergency Medical Response, and National Institute of Communicable Diseases).

LABORATORY TESTS

Samples should be tested in biosafety level (BSL)-3 or BSL 2+ laboratory with BSL-3 precautions. The apex laboratories are the National Institute of Communicable Diseases and the National Institute of Virology. There is a network of 16 other laboratories that can test for influenza A H1N1. This network is being expanded to include private laboratories. The updated list is available on the website of Ministry of Health and Family Welfare.[3]

INFECTION CONTROL MEASURE GUIDELINES

Infection control measures would be targeted according to the risk profile.[41,46]

Health Facility Management of Human Cases of Influenza A H1N1. During prehospital care, standard precautions should be followed when transporting a patient to a health care facility. The patient should be given a 3-layer surgical mask to wear. Aerosol-generating procedures should be avoided during transportation as much as possible. The personnel in the patient cabin of the ambulance should wear a full complement of PPE, including N95 masks; the driver should wear a 3-layer surgical mask.

Once the patient is admitted to the hospital, the interior and exterior of the ambulance and any reusable patient care equipment must be sanitized using sodium hypochlorite/quaternary ammonium compounds. Recommended procedures for disposal of waste (including PPE used by personnel) generated in the ambulance while transporting the patient should be followed.[48,49]

During the hospital stay, the patient should be admitted directly to the isolation facility and continue to wear the surgical mask. The identified medical, nursing, and paramedical personnel attending the patient should wear a full complement of PPE. If splashing with blood or other body fluids

Annals of Global Health, VOL. 81, NO. 5, 2015
September–October 2015: 645–653

is anticipated, a waterproof apron should be worn over the PPE.

Aerosol-generating procedures such as endotracheal intubation, nebulized medication administration, induction and aspiration of sputum or other respiratory secretions, airway suction, chest physiotherapy, and positive pressure ventilation should be performed by the treating physician or nurse, who should be wearing full complement of PPE with an N95 respirator.[48,49]

Sample collection and packing should be done under full cover of PPE with N-95 respirator. Hand hygiene must be performed before and after patient contact and after contact with contaminated items, whether or not gloves are worn. Until further evidence is available, infection control precautions should continue in an adult patient for 7 days after resolution of symptoms and 14 days after resolution of symptoms for children younger than 12 years because of longer period of viral shedding expected in children. The patient can return home, after resolution of fever, provided the he or she and household members follow recommended infection control measures and community health workers are available to monitor the patient.[48]

Because the virus can survive in the environment for variable periods of time (hours to days), cleaning, followed by disinfection, should be done for contaminated surfaces and equipment. The virus is inactivated by a number of disinfectants such as 70% ethanol, 5% benzalkonium chloride (Lysol), and 10% sodium hypochlorite. Patient rooms and areas should be cleaned at least daily and finally after the patient is discharged. In addition to daily cleaning of floors and other horizontal surfaces, special attention should be given to cleaning and disinfecting frequently touched surfaces. To avoid possible aerosolization of the virus, damp sweeping should be performed. Horizontal surfaces should be dusted by moistening a cloth with a small amount of disinfectant.[48,49] Heavily soiled equipment should be cleaned and then a disinfectant effective against influenza virus (mentioned previously) should be applied before removing it from the isolation room or area. If possible, contaminated patient care equipment should be placed in suitable bags before removing it from the isolation room or area.

When transporting contaminated patient care equipment outside the isolation area, gloves should be worn and hand hygiene should take place when transport is completed. Standard precautions should be taken and current recommendations for cleaning and disinfection or sterilization of reusable patient care equipment should be followed.

All waste generated from influenza patients in isolation should be considered clinical infectious waste and should be treated and disposed of in accordance with national regulations pertaining to such waste. When transporting waste outside the isolation area, gloves should be used, followed by hand hygiene.[48,49]

Standard Operating Procedures on Use of PPE. PPE reduces the risk for infection when used correctly. PPE includes nonsterile gloves; a high-efficiency mask or 3-layer surgical mask; long-sleeved, cuffed gown; protective eyewear (ie, goggles/visors/face shields); a cap, which may be used in high-risk situations where there may be increased aerosols; and a plastic apron if splashing of blood, body fluids, excretions, and secretions is anticipated.[50-53] The PPE should be used in situations where regular work practice requires unavoidable, relatively close contact with the suspected patient or with poultry.

PPE should be applied in the following order:

1. Wash hands thoroughly.
2. Put on the coverall.
3. Put on the goggles, shoe covers, and head cover in that order.
4. Put on a face mask (masks should be changed every 6-8 hours).
5. Put on gloves.[48,49]

PPE should be removed in the following order

1. Remove the gown and place in garbage bin.
2. Peel gloves from hand and discard.
3. Wash hands with soap and water or apply an alcohol-based hand rub
4. Remove cap and face shield: Place cap in bin and if reusable, place face shield in container for decontamination.
5. Remove mask by grasping elastic behind ears; do not touch front of mask.
6. Use alcohol-based hand rub or wash hands with soap and water.
7. Leave the room.
8. Once outside room use alcohol hand rub again or wash hands with soap and water.
9. Used PPE should be handled as per waste management protocol.[48,49]

GUIDELINES AND OPERATING PROCEDURES FOR INFECTION CONTROL PRACTICES

Infection Control Measures on the Individual Level.[46,48] Hand hygiene. Hand hygiene is the single most important measure for reducing the risk for

transmitting infectious organism from one person to other. Hands should be washed frequently with soap and water, alcohol-based hand rubs, or antiseptic hand wash and thoroughly dried preferably using disposable tissue or paper towels, after contact with respiratory secretions or contaminated surfaces. Any activity that involves hand-to-face contact such as eating, normal grooming, and smoking should be followed by thorough hand hygiene measures.[39,41]

Respiratory hygiene/cough etiquette. The following measures for containing respiratory secretions are recommended for all individuals with signs and symptoms of influenza-like illness.

1. Cover the nose and mouth with a handkerchief or tissue paper when coughing or sneezing.
2. Use tissues to contain respiratory secretions and dispose of the tissues in the nearest waste receptacle after use.
3. Perform hand hygiene (eg, hand washing with non-antimicrobial soap and water, alcohol-based hand rub, or antiseptic hand wash) after contact with respiratory secretions and contaminated objects/materials.[44,46]

Staying away. Stay an arms length away from individuals showing symptoms of influenza-like illness.

Use of mask. A 3-layer surgical mask is recommended for medical personnel working in screening areas and in isolation facilities and for medical personnel working in isolation wards or critical care facilities performing aerosol-generating procedures such as suction, endotracheal intubation, and so on.[39,41]

Infection Control Measures at a Health Facility. Droplet precautions. Health care personnel should observe droplet precautions (ie, wear a surgical or procedure mask for close contact), in addition to standard precautions, when examining a patient with symptoms of a respiratory infection, particularly when fever is present. These precautions should be maintained until it is determined that the cause of symptoms is not an infectious agent that requires droplet precautions.[46,48,49]

Visual alerts. Visual alerts (in appropriate languages) should be posted at the entrance to outpatient facilities (eg, emergency departments, physician offices, outpatient clinics). The alerts should instruct patients and persons who accompany them (eg, family, friends) to inform health care personnel of symptoms of a respiratory infection when they first register for care and to practice respiratory hygiene/cough etiquette.[46,48,49]

Use of PPE. The medical personnel, nurses, and paramedics attending the patient should wear a full complement of PPE. N-95 masks should be worn during aerosol-generating procedures. Hand hygiene should be performed before and after patient contact and after contact with contaminated items, even if gloves are worn. Sample collection and packing should be done under full cover of PPE.[46,48,49]

Decontaminating contaminated surfaces, fomites, and equipment. Cleaning, followed by disinfection, should be done for contaminated surfaces and equipment. Phenolic disinfectants, quaternary ammonia compounds, alcohol, or sodium hypochlorite should be used. Patient areas should be cleaned at least daily and terminally after discharge. In addition to daily cleaning of floors and other horizontal surfaces, special attention should be given to cleaning and disinfecting frequently touched surfaces. To avoid possible aerosolization of Avian influenza virus, damp sweeping should be performed. Heavily soiled equipment should be cleaned and a disinfectant effective against influenza virus should be applied before removing the equipment from the isolation area. When transporting contaminated patient care equipment outside the isolation area, gloves should be worn and proper hand hygiene should be undertaken once gloves are removed. Standard precautions and current recommendations for cleaning and disinfection or sterilization of reusable patient care equipment should be followed.[46,49]

Waste disposal. All waste must be treated as infectious and decontaminated as per standard procedures. Articles such as swabs and gauges should be discarded in yellow autoclavable biosafety bags after use. The bags must be autoclaved followed by incineration of their contents. Waste such as used gloves, face masks, and disposable syringes should be discarded in blue or white autoclavable biosafety bags, which should be autoclaved or microwaved before disposal. All hospital and laboratory personnel should follow the standard guidelines (Biomedical Waste Management and Handling Rules, 1998) for waste management.[46,48,49]

DISCUSSION

Sequence analysis of the 1918 Spanish influenza virus genes have not revealed any obvious features that could account for its high virulence thus far. Analyses of the surface proteins of the 1918 pandemic strain, however, suggest that this strain may have had a different origin. The hemagglutinin gene segment of the virus may have come directly from an avian source different from those currently circulating. Alternatively, the virus, or some of its

Annals of Global Health, VOL. 81, NO. 5, 2015
September–October 2015: 645–653

gene segments, may have evolved in an intermediate host before emerging as a human pathogen. Determining whether pandemic influenza virus strains can emerge via different pathways will affect the scope and focus of surveillance and prevention efforts. The key prevention strategy for reducing influenza pandemic-associated morbidity and mortality will be the implementation of inactivated influenza virus vaccines effective against the pandemic strain. Zanamivir and oseltamivir block influenza neuraminidase and prevent the cleavage of sialic acid residues, thus interfering with progeny virus dispersal within the mucosal secretions and reducing viral infectivity. Current surveillance efforts focused on rapid identification of novel strains in humans as well as efforts to minimize the possibility of cross-infection between species are aimed at detecting and preventing a new pandemic.

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