International Society of Heart and Lung Transplantation Advisory Statement on the Implications of Pandemic Influenza for Thoracic Organ Transplantation

This advisory statement has been produced by the **International Society of Heart and Lung Transplantation** to complement existing official guidance from national and international public health agencies. Please refer to your local and/ or national guidance and use this statement as complementary expert opinion on optimal management of patients pre and post thoracic organ transplantation in preparation for or during an outbreak of Pandemic Influenza.

This statement has been prompted by the identification of a novel swine influenza A (H1N1) virus causing illness in humans in Mexico, the United States, in multiple countries in Europe, Asia, Central and South America, Australia and New Zealand. The World Health Organization (WHO) and the US Centre for Disease Control (CDC) began monitoring this pandemic spread in real time on April 20, 2009, with updates on their websites daily. The pandemic threat is currently at Alert Level 5 (sustained community level outbreaks with person-to-person spread in at least 2 countries within one WHO region) which is a strong signal that a pandemic is imminent, according to the WHO. This Alert Level will be revised by the WHO in accordance with rates of spread around the world.

This Statement is relevant to:

Candidates Awaiting Heart or Lung or Heart-Lung Transplantation
Patients on Mechanical Circulatory Support (MCS)
Heart and Lung and Heart-Lung Transplant Recipients
Assessment of potential thoracic donor organs

Clinical Presentation

- Recognised symptoms of influenza infection include fever, headache, tiredness, cough, sore throat, runny nose, body aches, diarrhoea, and vomiting. These are non-specific and have similarities to seasonal, non-pandemic influenza and other community acquired respiratory virus infections.

- Conditions which historically increase the risk of severe influenza infection include chronic pulmonary, cardiovascular, renal, hepatic, hematological, or metabolic disorders and an immunosuppressed state.

- There remain many unknowns about behavior of pandemic influenza virus in the pre and post heart or lung transplant population and MCS patient population. The symptoms may present differently, the incubation period may be longer or shorter and the infection may be more or less severe.

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Reducing Risk of Influenza Infection using Basic Infection Control Approaches

- Personal distancing: stay at least 3 feet (1 meter) or arms length from everyone and when in public places, stay in well ventilated areas only.
- Cough etiquette: cough or sneeze into disposable tissue and dispose of immediately or if unavailable cough into axilla rather than onto hands.
- Hand washing: wash hand after touching anyone or anything and use alcohol rubs with intermittent soap and water scrubs for 20 seconds duration throughout the day.
- Monitor local community risk – News channels, national or international public health agency websites.
- If pandemic influenza is present in the local community then avoid public gatherings and avoid exposure to persons with non-specific illness.
- Remain up to date on other vaccines such as pneumococcal vaccination

Use of Face Masks by Immunosuppressed Patients in Public

- Surgical-style face masks might decrease episodes of contaminated hands reaching nose / mouth area with subsequent reduction in infection risk
- Masks are thought to have some limited efficacy in reducing the exposure to infectious droplets
- Masks should be worn by any infected patient and by a caretaker who is within 3 feet of an infected person
- Correctly fitted masks are required by health care workers engaged in the assessment or care of patients with suspected or proven pandemic influenza infection.

Practical Issues for Consideration

Designated Caregivers: Patient groups should clearly identify an adequate support system. This includes a home caregiver for pre or post thoracic organ transplant recipients or MCS patients and/ or family members should they also become infected.

Medication: Patients should ensure that they have adequate supplies of routine daily medications especially maintenance immunosuppression for transplant recipients and other essential treatment for chronic diseases like CHF, COPD, diabetes and hypertension, to last until a pandemic is over (up to 4 weeks if possible).

Travel: Non essential travel should be avoided by pre and post thoracic organ transplantation patients when an influenza pandemic is threatened. The pandemic alert level of 5 reflects that a

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pandemic is imminent. Data on community levels of infection with pandemic influenza is likely to lag by at least 2-3 days. There cannot be certainty that a travelers destination will be infection-free prospectively. Historically, if a patient travels to an area of significant community incidence of an infection, they will be at higher risk of contracting the illness. Additionally they may have a more severe illness and bring the illness back to their home community. At this point, the specific behavior of the Influenza A (H1N1) is unknown, but the consequences of illness thus far have included fatalities, as of 05/11/09, there have been 4694 cases with 54 deaths worldwide.

Managing Suspected Exposure or Suspected Infection

Patients pre and post thoracic organ transplantation and MCS patients are considered a "high-risk" group for complications of pandemic influenza virus infection. If a patient believes they have been exposed to a case of influenza they should consult their local healthcare provider to assess the need for testing and evaluation for possible anti-influenza treatment or prophylaxis. The patient must also inform their transplant or MCS centre. **Patients must not present to their healthcare provider or transplant centre unannounced in this situation**. The 2008-2009 seasonal influenza vaccine is not believed to offer protection against the Pandemic Influenza A H1N1 virus.

Antiviral chemoprophylaxis

Pre and post transplant recipients and MCS patients, both adults and pediatric, who are close contacts of a person or persons with probable or confirmed pandemic influenza A (H1N1) should receive antiviral chemoprophylaxis with either Oseltamivir (Tamiflu) or Zanamivir (Relenza) antiviral agents in accordance with their national guidance.

If seasonal influenza is still active in the patient's community, Zanamivir (Relenza) or Oseltamivir (Tamiflu) plus rimantadine or amantadine should be used to provide adequate empiric treatment or chemoprophylaxis for immunosuppressed patients that might have either the Pandemic Influenza A (H1N1) of swine origin or the seasonal human Influenza A (H1N1) virus infection- a known potentially lethal virus in this population.

Post-exposure antiviral chemoprophylaxis (Post EAC)

- A full risk assessment of the likelihood of exposure and the likely benefit of Post EAC to the patient should be performed.
- If appropriate, treat with antiviral(s) at prophylactic dosing for 10 days after the last known exposure to a symptomatic confirmed case of pandemic influenza infection.
- Post exposure prophylaxis should be considered for contacts during the infectious period (defined as 1 day before until 7 days after the case's onset of symptoms). However, the actual infectious period for the Pandemic Influenza A (H1N1) is, as yet, unknown.
- If the contact with a known case occurred more than 7 days earlier, then prophylaxis is not

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necessary.

Pre--exposure protection

- The use of pre-exposure chemoprophylaxis in high risk populations during an influenza pandemic is controversial due to the potential for the development of resistance to anti-viral agents. Local or national policy should be followed.

Actions for the patient during suspected or proven influenza infection

- Stay at home. Patients with Pandemic influenza A (H1N1) should receive treatment with antiviral agents. If patient is concerned about their condition, they should contact their healthcare provider and transplant center to report symptoms and get advice.

- Hospitalization should occur if the physician has any doubt about patient's ability to take medications, remain hydrated, or if they are developing respiratory insufficiency or other complications.

- Continue basic infection control measures in the home.

Actions for physicians during suspected or proven influenza infection:

- It is reasonable to initiate anti-viral treatment after diagnostic specimens have been obtained, even if symptoms have been present for >48 hours. The data that antiviral medication needs to be initiated within 48 hours of symptoms developing to have any effect applies to the non-immunosuppressed population.

- Use Oseltamivir 75 mg po bid or Zanamivir 10 mg (2 x 5mg blisters) inhaled bid for 5 days or until symptoms resolve, whichever is longer.

- If seasonal human Influenza A (H1N1) is also in the community, see above section on **antiviral chemoprophylaxis** and follow local and international recommendations.

- Physician may elect to attenuate immunosuppression during active infection. This decision should be individualized for each transplant patient by their transplant physician/team.

- Monitor recipients closely for allograft rejection and for co-infections such as Cytomegalovirus activation or Pneumocystis jiroveci pneumonia (PCP) infection.

- Illness might progress rapidly. Physicians should be vigilant for secondary bacterial infections including pneumonia.

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Drug interactions

- Oseltamivir and Zanamivir do not have drug interactions with ciclosporine, tacrolimus, mycophenolate, prednisone or sirolimus. There are no expected interactions with monoclonal antibody induction agents or anti- thymocyte globulin. Oseltamivir needs to be adjusted for renal impairment and Zanamivir should not be given to patients with COPD or at risk of bronchospasm.
- Rimantadine and Amantadine have a significant toxicity profile and should be given only with expert guidance. Care with drug interactions and monitoring for adverse effects of these drugs is needed if used in treatment or prophylaxis in this population.

Assessment of Thoracic Organ Donors during Pandemic Influenza A (H1N1)

- The risk assessment for any potential organ donor must be made at a local level with specific input from ID or clinical microbiology specialists within the transplant unit.
- Potential organ donors, who have been diagnosed as having influenza, either clinically or by virological diagnosis, should not be used as lung donors.
- Potential organ donors who have been diagnosed as having influenza but have received appropriate anti-viral therapy could be considered as potential heart donors.
- In potential organ donors who die of other causes – a careful medical/social history should be taken to determine if influenza symptoms were experienced by the patient. In such cases expert ID or clinical microbiology advice should be obtained prior to organ procurement.
- Since the full virulence of pandemic influenza is not known, careful consideration should be given to organ procurement in the presence of suspected infection.

These recommendations may be applied to patients pre and post thoracic organ transplantation, MCS patients, and their transplant teams in preparation for or during an outbreak of ANY pandemic influenza viral strain. Transplant teams must realize however that the clinical presentation and the antiviral treatment recommendations may vary from strain to strain and local public health agency guidance should be followed.

This statement was released jointly by
the International Society for Heart and Lung Transplantation's Education Committee and Scientific Council for Infectious Diseases
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