INFLUENZA

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Acute respiratory tract infection accompanied by systemic symptoms mainly fever, malaise, coryza, and myalgia. It is caused by an influenza virus belonging to the orthomyxoviridae group. Three types of Influenza viruses occur in humans i.e. Influenza A, B, and C

All the known pandemics were caused by influenza A strains as it is known to change its genetic makeup. Influenza B is comparatively a genetically stable virus without any animal reservoir and Influenza C causes a milder disease. There is one more type, influenza D which occurs exclusively in cattle.

The type A viruses are further divided into various subtypes based on the hemagglutinin “H” and neuraminidase “N” antigen expressed on their surface. There are 18 subtypes of hemagglutinin and 11 subtypes of neuraminidase.

Influenza epidemics affect 10-20% of the global population on an average each year and are typically the result of minor antigenic variations of the virus or “antigenic drift”, which occur often in influenza A virus. On the other hand, pandemics that are associated with higher mortality appear at longer and varying intervals (often many decades) as a consequence of major genetic reassortment of the virus “antigenic shift” as occurred during the Spanish flu pandemic H1N1 virus of 1918. Pigs are susceptible to avian,

human and swine influenza viruses, they potentially may be infected from influenza viruses from different species (e.g. ducks and humans) at the same time. If this happens, it is possible for the genes of the viruses to mix and create a new virus. As discussed above, this type of major change in the influenza A virus is known as antigenic shift. If this new virus causes illness in people and can be transmitted easily from person-to-person, an influenza pandemic can occur. This is what happened in 2009 when influenza A H1N1 virus with swine, avian and human genes emerged in the spring of 2009 and caused the first pandemic in more than 40 years.

Symptoms and signs

Type A and B seasonal influenza viruses produce clinically indistinguishable infections, whereas type C usually causes a mild illness. The incubation period is 1 - 4 days. In unvaccinated persons, uncomplicated influenza often begins abruptly. Symptoms range widely from nearly asymptomatic to a constellation of systemic symptoms (including fever, chills, headache, malaise, and myalgias)

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and respiratory symptoms (including runny/stuffy nose, sore throat, hoarseness, cough, and substernal soreness). Gastrointestinal symptoms and signs may occur, particularly among young children with influenza B virus infections. Fever lasts 1 - 7 days (usually 3 - 5). Elderly patients especially may present with lassitude and confusion, often without fever or respiratory symptoms. Signs include mild pharyngeal injection, flushed face, and conjunctival redness. Moderate enlargement of the cervical lymph nodes and tracheal tenderness may be observed. The presence of fever (higher than 38.2°C) and cough during the influenza season is highly predictive of influenza infection in those older than 4 years. Leukopenia is common and leukocytosis (especially more than 15000) may indicate a superadded bacterial infection.

Lab Testing

Rapid testing: Rapid influenza diagnostic tests for the

detection of influenza antigens from nasal or throat swabs are widely available. These tests are very quick (15- 30 min), highly specific but may have moderate to low sensitivity. Their sensitivity is strongly dependent on sample collection early in the course of illness, ideally within 48 hours of the onset of illness. Not all can differentiate between influenza A and Influenza B, and none can identify the subtypes of Influenza A.

PCR: More sensitive PCR techniques are available, although their sensitivity is compromised early in the season during low prevalence periods. A nasopharyngeal swab, nasal aspirate, combined nasopharyngeal swab with oropharyngeal swab, or material from a bronchoalveolar lavage can be tested for any influenza strain. When influenza pneumonia is suspected, lower respiratory tract specimens should be collected and tested for influenza viruses by RT-PCR.

Which patients to be tested for Influenza

IDSA Influenza Clinical Guidelines 2018

COMPLICATIONS:

- Acute viral pneumonia, respiratory failure, and shock
- Secondary bacterial infection/pneumonia
- Upper respiratory infections including acute sinusitis and otitis media
- Cardiovascular disease in particular among older adults and influenza is postulated to be a significant trigger for myocardial infarction, cerebrovascular disease, and sudden death. Several studies suggest that influenza vaccination has a protective effect against major adverse cardiovascular events.
- Neurologic complications, including seizures and encephalopathy, may occur.
- **Reye syndrome** (fatty liver with encephalopathy) is a rare and severe complication of influenza (usually B type) and other viral diseases (especially varicella), particularly in young children. It consists of rapidly progressive hepatic failure and encephalopathy, and there is a 30% mortality rate. The pathogenesis is unknown, but the syndrome is associated with aspirin use in the management of viral infections.

AT RISK POPULATION:

- Patients with asthma,
- Residents of nursing homes and long-term care facilities,
- Adults aged 65 years or older,
- Persons who are morbidly obese,
- Infection during pregnancy increases the risk for hospitalization and may be associated with severe illness, sepsis, pneumothorax and respiratory failure, spontaneous abortion, preterm labor, and fetal distress,
- Persons with underlying medical conditions (pulmonary, renal, cardiovascular, hepatic, hematologic, neurologic and neuro developmental conditions and immune-deficient conditions such as HIV)

TREATMENT:

Mainly supportive

Antiviral therapy should be considered for all persons with acute illness, in particular, those at high risk for developing complications who have a suggestive clinical presentation or with laboratory-confirmed influenza. A five-day course of antivirals is usually sufficient in most of the cases (see the drug table below).

Clinicians should administer post exposure antiviral chemoprophylaxis with Neuraminidase Inhibitors (inhaled zanamivir or oral oseltamivir) in a non outbreak setting for 7 days after the most recent exposure to close contact with influenza

Patient categories A, B or C MHFW guidelines on the categorization of Seasonal Influenza A (Revised on 11.02.2015)

At first, all individuals seeking consultations for flu-like symptoms should be screened at healthcare facilities both Government and private or examined by a doctor and these will be categorized as under:

Category-A

- Patients with mild fever (less than 38° C) plus cough / sore throat with or without body aches, headache, diarrhea, and vomiting will be categorized as Category-A. They do not require Oseltamivir and should be treated for the symptoms mentioned above. The patients should be monitored for their progress and reassessed at 24 to 48 hours by the doctor.
- No testing of the patient for Influenza is required.
- Patients should confine themselves at home and avoid mixing up with public and high-risk members in the family.

Category-B

(i) In addition to all the signs and symptoms mentioned under Category-A, if the patient has

high-grade fever (Above 38° C) and severe sore throat, may require home isolation and

Oseltamivir;

(ii) In addition to all the signs and symptoms mentioned under Category-A, individuals having one or more of the following high-risk conditions shall be treated with

Chemotherapy and chemoprophylaxis**Table 8. Antiviral Agents and Dosing Recommendations for Treatment and Chemoprophylaxis of Influenza**

Antiviral Agents and Age Group	Treatment Dosing	Chemoprophylaxis Dosing
Oseltamivir		
Adults	75 mg twice daily	75 mg once daily
Pregnancy (any trimester) ^a	75 mg twice daily ^b	75 mg once daily ^b
Children (1 year or older) ≤15 kg	30 mg twice daily	30 mg once daily
Children >15–23 kg	45 mg twice daily	45 mg once daily
Children >23–40 kg	60 mg twice daily	60 mg once daily
Children >40 kg	75 mg twice daily	75 mg once daily
Infants 9–11 months	3.5 mg/kg per dose twice daily ^c	3.5 mg/kg per dose once daily ^c
	3 mg/kg per dose twice daily ^c	3 mg/kg per dose once daily ^c
Term infants 0–8 months	3 mg/kg per dose twice daily	3 mg/kg per dose once daily if ≥3 months; not recommended for infants <3 months unless the situation is judged critical due to lack of safety and efficacy data
Preterm infants	See details in footnote ^a	No data
Zanamivir		
Adults	10 mg (two 5-mg inhalations), twice daily	10 mg (two 5-mg inhalations), once daily
Children (≥7 years)	10 mg (two 5-mg inhalations), twice daily	10 mg (two 5-mg inhalations), once daily
Peramivir^d		
Adults	600 mg intravenous infusion once, given over 15–30 minutes	NA
Children (2–12 years)	One 12 mg/kg dose, up to 600 mg maximum, intravenous, given over 15–30 minutes	NA
Children (13–17 years)	600 mg intravenous infusion once, given over 15–30 minutes	NA

Antiviral resistance information is available in the weekly Centers for Disease Control and Prevention (CDC) influenza surveillance report: <https://www.cdc.gov/flu/weekly/index.htm>.

Oseltamivir:

- Children with mild illness but with predisposing risk factors.
- Pregnant women;
- Persons aged 65 years or older;
- Patients with lung diseases, heart disease, liver disease, Kidney disease, blood disorders, diabetes, neurological disorders, cancer, and HIV/AIDS;
- Patients on long term cortisone therapy.
- No test for Influenza is required for Category-B (i) and (ii).
- All patients of Category-B (i) and (ii) should confine themselves at home and avoid mixing with public and high-risk members in the family.
- Broad Spectrum antibiotics as per the Guideline for Community-acquired pneumonia (CAP) may be prescribed wherever indicated.

Category-C

In addition to the above signs and symptoms of

Category-A and B, if the patient has one or more of the following:

- Breathlessness, chest pain, drowsiness, fall in blood pressure, sputum mixed with blood, bluish discoloration of nails;
- Children with influenza-like illness who had a severe disease as manifested by the redflag signs (Somnolence, high and persistent fever, inability to feed well, convulsions, shortness of breath, difficulty in breathing, etc).
- Worsening of underlying chronic conditions.

All these patients mentioned above in Category-C require testing, immediate hospitalization, and treatment.

Prevention/prophylaxis**Influenza Vaccines:**

The trivalent influenza vaccine contains three different vaccine viral antigens, one each from an influenza A(H1N1) virus, influenza A (H3N2) Virus, and an influenza B virus. **Quadrivalent** influenza vaccine contains the same three antigens as trivalent vaccines, along with an antigen from a second influenza B vaccine virus strain. **Minimum age:** 6

months for inactivated influenza vaccine [IIV] or recombinant influenza vaccine [RIV], 2 years for **live attenuated influenza vaccine [LAIV]**.

Routine vaccination:

Although annual influenza vaccination is recommended for all individuals aged 6 months or more, vaccination efforts should focus on individuals who:

- 1) Are 6-59 months of age
- 2) Are 50 years or more in age
- 3) Have chronic pulmonary (including asthma), cardiovascular (except isolated hypertension), renal, hepatic, hematologic (including sickle cell disease), metabolic (including diabetes mellitus), or neurologic (disorders of the brain and spinal cord, cerebral palsy, epilepsy, stroke, intellectual disability, moderate to severe developmental delay, muscular dystrophy, spinal cord injury) disorders
- 4) Are Immunocompromised due to any cause (including drug-induced, HIV, etc.)
- 5) Are or plan to be pregnant during the influenza season
- 6) Are 6 months to 18 years of age and receiving aspirin or salicylate-containing medications (and may be at risk for Reye syndrome after influenza virus infection)
- 7) Are residents of nursing homes or other long-term care facilities
- 8) Are Native Americans, including Alaska natives
- 9) Are extremely obese (BMI of 40 or more)
- 10) Are health care personnel who have the potential for exposure to patients and/or to infectious materials
- 11) Are household contacts (including children) or care givers of children < 5 years or adults aged 50 years or more, particularly contacts of children < 6 months
- 12) Are house contacts (including children) or caregivers of persons with medical conditions that put them at increased risk for severe complications of influenza?

For most healthy, non-pregnant persons aged 2 through 49 years, LAIV, IIV or RIV may be used. However, LAIV should NOT be administered to some persons, including:

- 1) children younger than 2 years and adults 50 years or

older

- 2) persons who have experienced severe allergic reactions to LAIV, any of its components, or to any previous dose of any other influenza vaccine;
- 3) children 2 through 17 years receiving aspirin or aspirin-containing products;
- 4) persons who are allergic to eggs;
- 5) pregnant women;
- 6) immunosuppressed persons;
- 7) children 2 through 4 years of age with asthma or who had wheezing in the past 12 months.
- 8) Persons who have taken influenza antiviral medications in the previous 48 hours.
- 9) People who care for severely immunocompromised persons who require a protected environment (or otherwise avoid contact with those persons for 7 days after getting the nasal spray vaccine)

For children aged 6 months through 8 years:

Administer 2 doses (separated by at least 4 weeks) to children who are receiving influenza vaccine for the first time.

For persons aged 9 years and older:

Administer 1 dose.

Timing of Vaccination:

Vaccination should be offered by the end of October, however, should continue to be offered as long as influenza viruses are circulating and unexpired vaccine is available

Children aged 6 months through 8 years who require 2 doses should receive their first dose as soon as possible after vaccine becomes available, and the second dose 4 weeks later

Acknowledgments:

Ministry of Health & Family Welfare Guidelines on the categorization of Seasonal Influenza A H1N1 cases (Revised on 11.02.2015)

Centers for Disease Control, the official website

Current Medical Diagnosis and Treatment 2019

Harrison's Principles of Internal Medicine 20th Edition

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