**INFLUENZA**

<http://www.accesspharmacy.com.libproxy.temple.edu/content.aspx?aID=8002175>

*Influenza is a viral illness associated with high mortality and high hospitalization rates among persons older than age 65 years. The aging of the population is contributing to an increased disease burden in the United States.*

Significant morbidity and mortality among young children, and the elderly

Vaccination is the primary mechanism of prevention of influenza in the United States

The highest rate of infection occurs in children, but the highest rates of severe illness, hospitalization, and death occur among those older than age 65 years, young children (<2 years old), and those who have underlying medical conditions, including pregnancy and cardiopulmonary disorders, that increase their risk of complications from influenza

Deaths associated with influenza often result from secondary bacterial pneumonia, primary viral pneumonia, and/or exacerbation of underlying [comorbidities](javascript:PopupGlossaryTerm(2753122);).

Among influenza A, B & C, Influenza A and B viruses are the two types that cause disease in humans. Influenza A viruses are responsible for the regular, seasonal [epidemics](javascript:PopupGlossaryTerm(2752252);) of the flu, whereas influenza B viruses are typically associated with sporadic [outbreaks](javascript:PopupGlossaryTerm(2752239);), particularly among residents of long-term care facilities

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Influenza A viruses are responsible for the regular, seasonal [epidemics](javascript:PopupGlossaryTerm(2752252);) of the flu

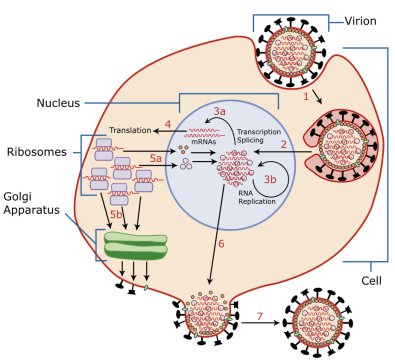
Two subtypes based on changes in two surface antigens:

* [Hemagglutinin](javascript:PopupGlossaryTerm(2753322);) allows the influenza virus to enter host cells by attaching to sialic acid receptors and is the major antigen to which antibodies are directed upon exposure
  + 16 hemagglutinin subtypes (H1 – H16) …. **Only H1 & H3 are pandemic**
* [Neuraminidase](javascript:PopupGlossaryTerm(2753521);) allows the release of new viral particles from host cells by catalyzing the cleavage of linkages to sialic acid
  + 9 neuraminidase subtypes (N1 – N9) … **Only N1 & N2 are pandemic**

Influenza B viruses are typically associated with sporadic [outbreaks](javascript:PopupGlossaryTerm(2752239);), particularly among residents of long-term care facilities – NO subtypes

<http://en.wikipedia.org/wiki/Influenza>

HA – NA – M2



Influenza viruses bind through [hemagglutinin](http://en.wikipedia.org/wiki/Hemagglutinin) onto [sialic acid](http://en.wikipedia.org/wiki/Sialic_acid) sugars on the surfaces of [epithelial cells](http://en.wikipedia.org/wiki/Epithelium), typically in the nose, throat, and [lungs](http://en.wikipedia.org/wiki/Lung) of mammals, and [intestines](http://en.wikipedia.org/wiki/Intestine) of birds (Stage 1 in infection figure).[[58]](http://en.wikipedia.org/wiki/Influenza#cite_note-Wagner-57) After the hemagglutinin is [cleaved](http://en.wikipedia.org/wiki/Proteolysis) by a [protease](http://en.wikipedia.org/wiki/Protease), the cell imports the virus by [endocytosis](http://en.wikipedia.org/wiki/Endocytosis)

Once inside the cell, the acidic conditions in the [endosome](http://en.wikipedia.org/wiki/Endosome) cause two events to happen: First, part of the hemagglutinin protein fuses the [viral envelope](http://en.wikipedia.org/wiki/Viral_envelope) with the vacuole's membrane, then the M2 [ion channel](http://en.wikipedia.org/wiki/Ion_channel) allows [protons](http://en.wikipedia.org/wiki/Proton) to move through the viral envelope and acidify the core of the virus, which causes the core to dissemble and release the viral RNA and core proteins.[[51]](http://en.wikipedia.org/wiki/Influenza#cite_note-Bouvier-50) The viral RNA (vRNA) molecules, accessory proteins and [RNA-dependent RNA polymerase](http://en.wikipedia.org/wiki/RNA-dependent_RNA_polymerase) are then released into the [cytoplasm](http://en.wikipedia.org/wiki/Cytoplasm) (Stage 2).

These core proteins and vRNA form a complex that is transported into the [cell nucleus](http://en.wikipedia.org/wiki/Cell_nucleus), where the RNA-dependent RNA polymerase begins transcribing complementary positive-sense vRNA (Steps 3a and b).

The vRNA either is exported into the cytoplasm and translated (step 4) or remains in the nucleus

Newly synthesized viral proteins are either secreted through the [Golgi apparatus](http://en.wikipedia.org/wiki/Golgi_apparatus) onto the cell surface (in the case of neuraminidase and hemagglutinin, step 5b) or transported back into the nucleus to bind vRNA and form new viral genome particles (step 5a)

Hemagglutinin and neuraminidase molecules cluster into a bulge in the cell membrane. The vRNA and [viral core](http://en.wikipedia.org/wiki/Capsid) proteins leave the nucleus and enter this membrane protrusion (step 6)

The mature virus buds off from the cell in a sphere of host [phospholipid membrane](http://en.wikipedia.org/wiki/Lipid_bilayer), acquiring hemagglutinin and neuraminidase with this membrane coat (step 7). As before, the viruses adhere to the cell through hemagglutinin; the mature viruses detach once their [neuraminidase](http://en.wikipedia.org/wiki/Neuraminidase) has cleaved sialic acid residues from the host cell

[Immunity](javascript:PopupGlossaryTerm(2752291);) to influenza virus occurs as a result of the development of antibody directed at the surface antigens, particularly [hemagglutinin](javascript:PopupGlossaryTerm(2753322);). However, immunity to one influenza subtype does not offer protection against other subtypes or types of influenza.

*Seasonal influenza* [*epidemics*](javascript:PopupGlossaryTerm(2752252);) *are the result of viral* [***antigenic drift***](javascript:PopupGlossaryTerm(2752985);)*, which is why the influenza* [*vaccine*](javascript:windowReference('drugInfo','drugClassification.aspx?catid=1733');) *is changed on a yearly basis. Antigenic drift forms the foundation of the recommendation for* ***annual*** *influenza vaccination.*

**ANTIGENIC DRIFT:** small changes in the hemagglutinin and/or [neuraminidase](javascript:PopupGlossaryTerm(2753521);) molecules

*The acquisition of a new* [*hemagglutinin*](javascript:PopupGlossaryTerm(2753322);) *and/or* [*neuraminidase*](javascript:PopupGlossaryTerm(2753521);) *by the influenza virus is called* [***antigenic shift***](javascript:PopupGlossaryTerm(2752986);)*, which results in a novel influenza virus that has the potential to cause a* [***pandemic***](javascript:PopupGlossaryTerm(2752353);)*.*

**ANTIGENIC SHIFT:** influenza virus acquires a **NEW** [hemagglutinin](javascript:PopupGlossaryTerm(2753322);) and/or [neuraminidase](javascript:PopupGlossaryTerm(2753521);) via genetic reassortment rather than point mutations.

***Clinical diagnosis of influenza is difficult***

Classic signs and symptoms include

* abrupt onset of fever
* muscle pain
* headache
* malaise
* nonproductive cough
* sore throat
* rhinitis

These signs and symptoms usually resolve within 1 week of presentation.

***Lab Tests***

* Complete blood count and chemistry panels should be obtained to assess the overall status of the patient.
* The gold standard for diagnosis of influenza is viral culture, which can provide information on the specific strain and subtype. Viral culture has a high sensitivity but can take as long as a week to develop, limiting the clinical relevance of the results.
* Tests such as the rapid antigen and point-of-care (POC) tests, direct fluorescence antibody (DFA) test, and the reverse-transcription polymerase chain reaction (RT-PCR) assay may be used for rapid detection of virus.

Seasonal influenza [vaccine](javascript:windowReference('drugInfo','drugClassification.aspx?catid=1733');) will not likely provide protection against the **novel influenza A (H1N1)** due to absence of or low levels of cross reacting antibodies. As a result, new **monovalent** live-attenuated (mLAIV) and inactivated **monovalent** influenza vaccine (MIV) formulations against the novel H1N1 virus are available ([Table 118–2](javascript:windowReference('Reference',%20'popup.aspx?aID=8002219');)).

Simultaneous administration of inactivated vaccines against seasonal and novel influenza A H1N1 is permissible if given at different sites. However, administration of live attenuated vaccine formulations against seasonal and novel H1N1 simultaneously is not recommended

The **trivalent** influenza vaccine (TIV) **by IM** and the live-attenuated influenza vaccine (LAIV) by **intranasal** are the two commercially available vaccines for prevention of seasonal influenza

Both vaccines contain influenza A subtypes H3N2 and H1N1 and influenza B virus, which are initially grown in **hens' eggs**.

TIV is [FDA](javascript:PopupGlossaryTerm(2752550);) approved for use in people older than 6 months of age, regardless of their immune status

Afluria (inactivated vaccine) is contraindicated in patients with hypersensitivity to [neomycin](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6637');) or polymyxin

Pregnant women, regardless of trimester, and immunocompromised patients should receive annual influenza vaccination with TIV but not with LAIV

*Antiviral drugs for prophylaxis of influenza should be considered adjuncts to vaccine and are not replacements for annual vaccination.*

The two classes of antiviral drugs available for influenza prophylaxis are the adamantanes and the [neuraminidase](javascript:PopupGlossaryTerm(2753521);) inhibitors ([**oseltamivir**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6690');) **and** [**zanamivir**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7176');)**)**. Adamantane monotherapy is currently not recommended for prophylaxis or treatment in the United States because of the rapid emergence of resistance

Both the adamantanes and the [neuraminidase](javascript:PopupGlossaryTerm(2753521);) inhibitors are excreted in breast milk and should be avoided by mothers who are breastfeeding their infants

[**Amantadine**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=5604');) **and** [**rimantadine**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6893');) are adamantanes that have activity against seasonal influenza A H1N1 only. The adamantanes block the M2 ion channel, which is specific to influenza A viruses, and inhibit viral uncoating. Rapid emergence of resistance is a problem with these agents because cross-resistance is conferred by a single point mutation, which is why adamanatane monotherapy is not recommended

[**Oseltamivir**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=6690');) **(> 1 yo) and** [**zanamivir**](javascript:windowReference('drugInfo','drugContentPopup.aspx?mid=7176');) **(> 7 yo)** are [neuraminidase](javascript:PopupGlossaryTerm(2753521);) inhibitors that have activity against both influenza A and influenza B viruses, although resistance to oseltamivir among seasonal influenza A H1N1 is on the rise.[26](http://www.accesspharmacy.com.libproxy.temple.edu/content.aspx?aID=8002339#8002339),[27](http://www.accesspharmacy.com.libproxy.temple.edu/content.aspx?aID=8002340#8002340) Without neuraminidase, release of the virus from infected cells is impaired, and thus, viral replication is decreased. When administered within 48 hours of the onset of illness, oseltamivir and zanamivir may reduce the duration of illness by approximately 1 day versus placebo

Pregnancy should not be considered a [contraindication](javascript:PopupGlossaryTerm(2751010);) to oseltamivir or zanamivir use

Zanamivir may be preferred because of its limited systemic absorption, but respiratory complications need to be considered, especially in women with underlying respiratory diseases.