Influenza & Vaccination

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CDC:

"As long as flu viruses are circulating, vaccination should continue, even in January or later."

Influenza

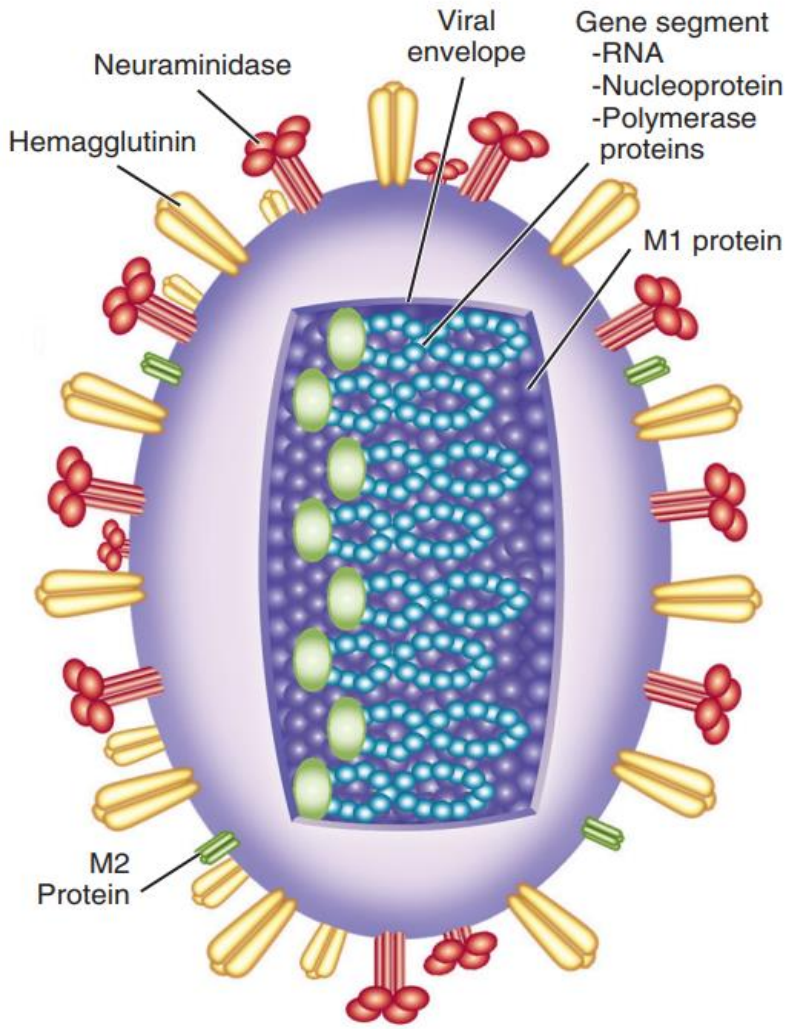
- Influenza (flu) is a contagious respiratory illness caused by influenza viruses that infect the nose, throat, and lungs. Some people, such as older people, young children, and people with certain health conditions, are at higher risk of serious flu complications. There are two main types of influenza (flu) viruses: **Types A and B**.

- The influenza A and B viruses that routinely spread in people (human influenza viruses) are responsible for seasonal flu epidemics each year.

Influenza

- Influenza viruses are enveloped, single-stranded RNA viruses whose genome is segmented.
- Four types (A, B, C and D) are recognized, with many subtypes within the type A viruses.
- H1 to H16
- N1 to N9

Influenza


Neuraminidase
Hemagglutinin
Viral envelope
Gene segment
-RNA
-Nucleoprotein
-Polymerase proteins
M1 protein
M2 Protein

	INFLUENZA A	INFLUENZA B	INFLUENZA C
Genetics	8 gene segments	8 gene segments	7 gene segments
Structure	10 viral proteins M2 unique	11 viral proteins NB unique	9 viral proteins HEF unique
Natural host range	Humans, swine, equine, birds, marine mammals[a]	Humans only	Humans and swine
Epidemiology	Antigenic shift and drift	Antigenic drift only; two main lineages cocirculate	Antigenic drift only; multiple variants
Clinical manifestations	May cause large pandemics with significant mortality in young persons	Severe disease generally confined to older adults or persons at high risk; pandemics not seen	Mild disease without seasonality

ANTIGENIC VARIATION

Antigenic Drift:

minor antigenic changes that occur frequently within the HA and/or NA of the virus.

(Drift is also a primary reason why the composition of flu vaccines for use in the Northern and Southern Hemispheres is reviewed annually.)

Antigenic Shift:

At unpredictable intervals, influenza A viruses with more radical changes in the antigenicity of the HA and/or NA have emerged to cause widespread disease, or pandemics.

Disease Impact

- In general, the level of excess mortality is highest when influenza A (H3N2) viruses predominate, but influenza B and to a lesser extent H1N1 viruses also can be associated with excess mortality.

Simonsen L, Clarke MJ, Williamson DW, et al. The impact of influenza epidemics on mortality: introducing a severity index. Am J Public Health. 1997;87:1944–1950.

Disease Impact

- Much of the impact of influenza is related to the malaise and consequent disability.

- It has been estimated that a typical case of influenza, on average, is associated with 5 to 6 days of restricted activity, 3 to 4 days of bed disability, and about 3 days lost from work or school.

- Economic impact

Risk of flu complications

- Adults 65 years and older
- Children younger than 2 years old
- Neurologic and neurodevelopment conditions
- Blood disorders (such as sickle cell disease)
- Chronic lung disease (such as chronic obstructive pulmonary disease [COPD] and cystic fibrosis, Asthma)
- Endocrine disorders (such as diabetes mellitus)
- Heart disease (such as congenital heart disease, congestive heart failure and coronary artery disease)

Risk of flu complications

- Kidney diseases
- Liver disorders
- Metabolic disorders (such as inherited metabolic disorders and mitochondrial disorders)
- People who are obese with a body mass index [BMI] of 40 or higher
- People younger than 19 years old on long-term aspirin- or salicylate-containing medications.
- People with a weakened immune system due to disease (such as people with HIV or AIDS, or some cancers such as leukemia) or medications (such as those receiving chemotherapy or radiation treatment for cancer, or persons with chronic conditions requiring chronic corticosteroids or other drugs that suppress the immune system)

people at higher risk from flu

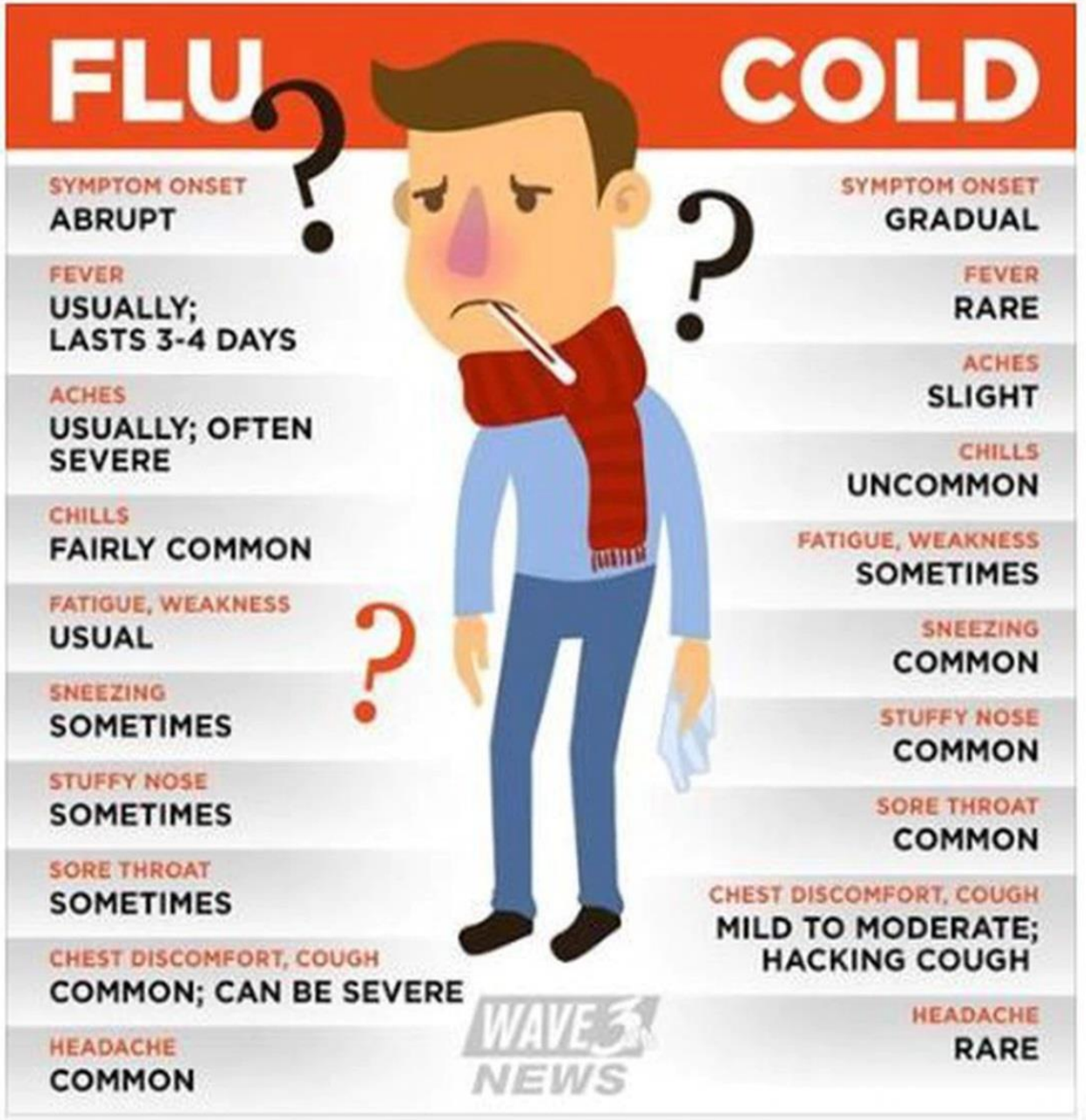
- Pregnant people and people up to 2 weeks after the end of pregnancy
- People who live in nursing homes and other long-term care facilities
- Although all children younger than 5 years old are considered at higher risk of serious flu complications, the highest risk is for those younger than 2 years old, with the highest hospitalization and death rates among infants younger than 6 months old.

Transmission

- Coughing and sneezing could generate small-particle aerosols (<10 µm mass diameter) that can remain suspended in air for many hours.
- Larger particles or droplets will typically fall to the ground within 2-3 meters of the infected person and would be expected to infect individuals in direct contact.
- Viral particles could land on surfaces, where influenza viruses remain infectious and could infect others through indirect contact.
- Incubation period: 1-4 days
- Shedding: Peaks at 1-2 days, and lasts 4.3-10 days?

CLINICAL FINDINGS

- Uncomplicated Influenza
- Pulmonary Complications
- Myositis
- Cardiac Complications
- Toxic Shock like Syndrome
- Central Nervous Complications: GBS, acute encephalitis and encephalopathy, transverse myelitis
- Reye Syndrome: Almost exclusively seen in children who have been given aspirin for treatment of febrile illnesses due to influenza and other viruses


FLU
COLD
SYMPTOM ONSET
ABRUPT
FEVER
USUALLY;
LASTS 3-4 DAYS
ACHES
USUALLY; OFTEN
SEVERE
CHILLS
FAIRLY COMMON
FATIGUE, WEAKNESS
USUAL
SNEEZING
SOMETIMES
STUFFY NOSE
SOMETIMES
SORE THROAT
SOMETIMES
CHEST DISCOMFORT, COUGH
COMMON; CAN BE SEVERE
HEADACHE
COMMON
SYMPTOM ONSET
GRADUAL
FEVER
RARE
ACHES
SLIGHT
CHILLS
UNCOMMON
FATIGUE, WEAKNESS
SOMETIMES
SNEEZING
COMMON
STUFFY NOSE
COMMON
SORE THROAT
COMMON
CHEST DISCOMFORT, COUGH
MILD TO MODERATE;
HACKING COUGH
HEADACHE
RARE
WAVE 3
NEWS


FLU
VS.
COVID-19
UnityPoint Health

Role of Viral Diagnosis in Clinical Decision Making

- Diagnostic testing should be used if the results of the test will influence subsequent clinical management.

This would include decisions regarding :

- The use of antiviral agents,
- The need for antibacterial drugs,
- Considerations for infection control.

Time to testing

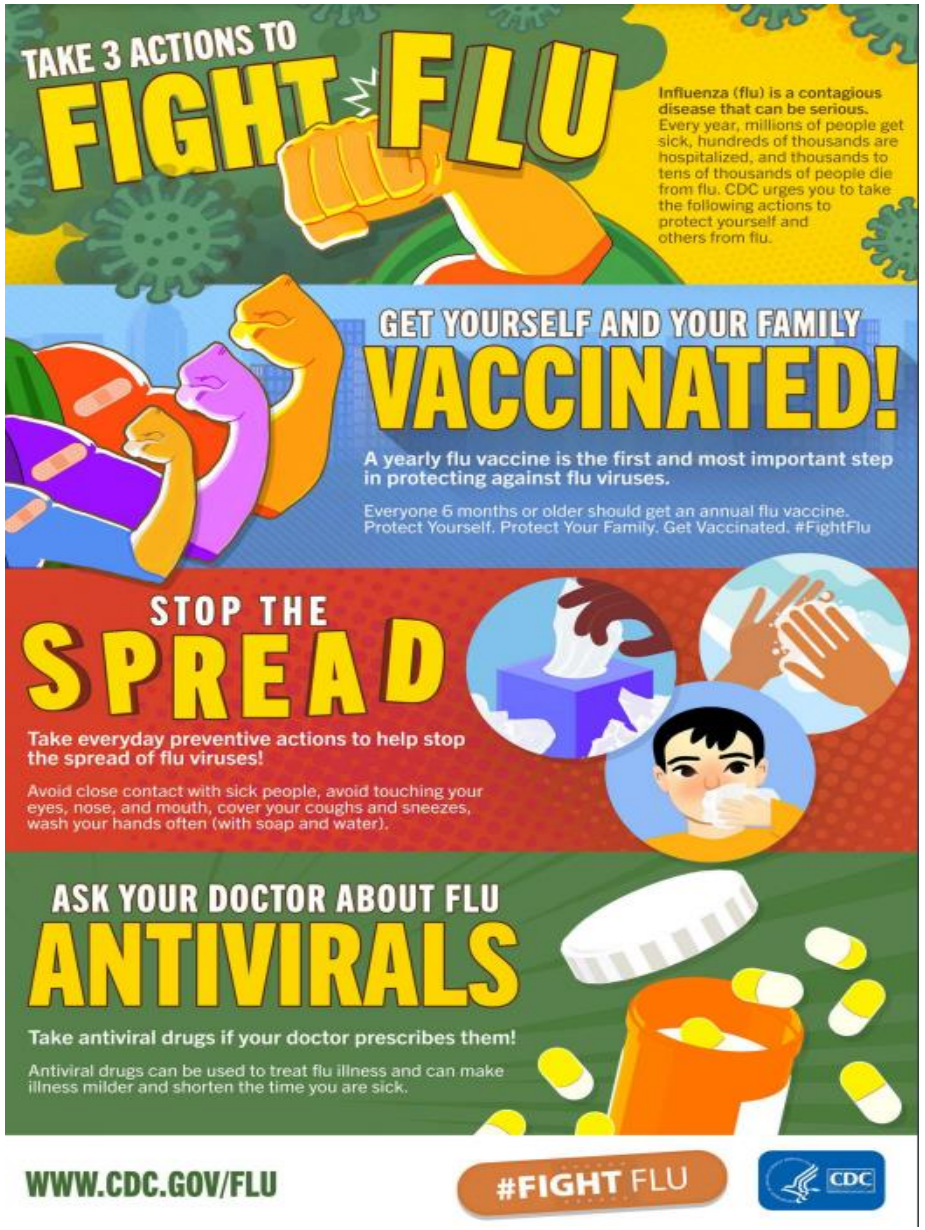
- Outpatients with higher risk for influenza complications should be considered for testing if they are presenting within 5 days of symptom onset.

- Outpatients who are immunocompromised, elderly, or infants may have prolonged shedding and could be considered for testing even beyond the 5-day window.

Time to testing

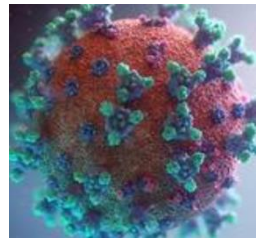
- Hospitalized patients with febrile illness during influenza epidemics should also be tested regardless of duration of symptoms, as should patients who develop febrile illnesses in hospital during influenza epidemics, to determine nosocomial transmission.

- patients who are not in one of these groups might undergo diagnostic testing as part of epidemiologic surveillance in the community.


TAKE 3 ACTIONS TO
FIGHT FLU
Influenza (flu) is a contagious disease that can be serious. Every year, millions of people get sick, hundreds of thousands are hospitalized, and thousands to tens of thousands of people die from flu. CDC urges you to take the following actions to protect yourself and others from flu.
GET YOURSELF AND YOUR FAMILY
VACCINATED!
A yearly flu vaccine is the first and most important step in protecting against flu viruses.
Everyone 6 months or older should get an annual flu vaccine. Protect Yourself. Protect Your Family. Get Vaccinated. #FightFlu
STOP THE
SPREAD
Take everyday preventive actions to help stop the spread of flu viruses!
Avoid close contact with sick people, avoid touching your eyes, nose, and mouth, cover your coughs and sneezes, wash your hands often (with soap and water).
ASK YOUR DOCTOR ABOUT FLU
ANTIVIRALS
Take antiviral drugs if your doctor prescribes them!
Antiviral drugs can be used to treat flu illness and can make illness milder and shorten the time you are sick.
WWW.CDC.GOV/FLU
#FIGHT FLU
CDC


Your work is essential!
Protect yourself & others from flu and COVID-19 this fall and winter:
MASK UP
Wear a face mask that covers your nose and mouth. And keep your distance (at least 6 feet) from others when you can.
LATHER UP
Wash your hands often with soap and water. If soap and water aren't available, use an alcohol-based hand sanitizer.
SLEEVE UP
Getting a flu vaccine is more important than ever. Everyone 6 months and older should get a flu vaccine every season.
A flu vaccine can protect you, your loved ones, and your co-workers from flu.
You can also protect those around you by staying home if you are sick.
Learn more at cdc.gov/flu
#FIGHT FLU
CDC

Preventive actions



- Avoid close contact with people who are sick.
- Cover coughs and sneezes.
- Cover your nose and mouth with a tissue when you cough or sneeze.
- Throw the tissue in the trash after you use it.
- Wash your hands often with soap and water, dry hands with a paper towel, and use the paper towel to turn off the faucet. If soap and water are not available, use an alcohol-based hand rub.

Preventive actions

- Avoid touching your eyes, nose, and mouth. Germs spread this way.

- Clean and disinfect surfaces and objects that may be contaminated with viruses that cause flu:

1-Most studies have shown that the flu virus can live and potentially infect a person for up to 48 hours after being deposited on a surface.

2- Letting it stand for 3 to 5 minutes.

Preventive actions

- CDC recommends that people stay home for at least 24 hours after their fever or signs of a fever (chills, feeling very warm, flushed appearance, or sweating) without the use of fever-reducing medicine, is gone.

- CDC recommends a yearly flu vaccine as the first and most important step in protecting against flu viruses.

- No time limitation for vaccination.

- Egg-based vaccine composition recommendations:
- an A/Victoria/2570/2019 (H1N1) pdm09-like virus;
- an A/Cambodia/e0826360/2020 (H3N2)-like virus;
- a B/Washington/02/2019- like virus (B/Victoria lineage);
- a B/Phuket/3073/2013-like virus (B/Yamagata lineage)
- Cell- or recombinant-based vaccine composition recommendations:
- an A/Wisconsin/588/2019 (H1N1) pdm09-like virus;
- an A/Cambodia/e0826360/2020 (H3N2)-like virus;
- a B/Washington/02/2019- like virus (B/Victoria lineage);
- a B/Phuket/3073/2013-like virus (B/Yamagata lineage).

- Serum antibodies peak between 2 and 4 weeks after vaccination but fall quickly, reaching near baseline before the next influenza season.

- Cellular responses, including CD4+ T-cell responses, are also noted and there is a strong correlation between the CD4 T-cell response and the antibody response.

Immune response to vaccine

- Although the induction of HAI antibody is generally accepted as a correlate of vaccine protection, in some populations such as the elderly it has been suggested that induction of cellular responses may also correlate with protection.

- Unimmunized young children generally require two doses of IIV given at least 4 weeks apart to generate substantial serum antibody responses.

Immune response to vaccine

- Both age and underlying conditions may contribute to these lowered responses.

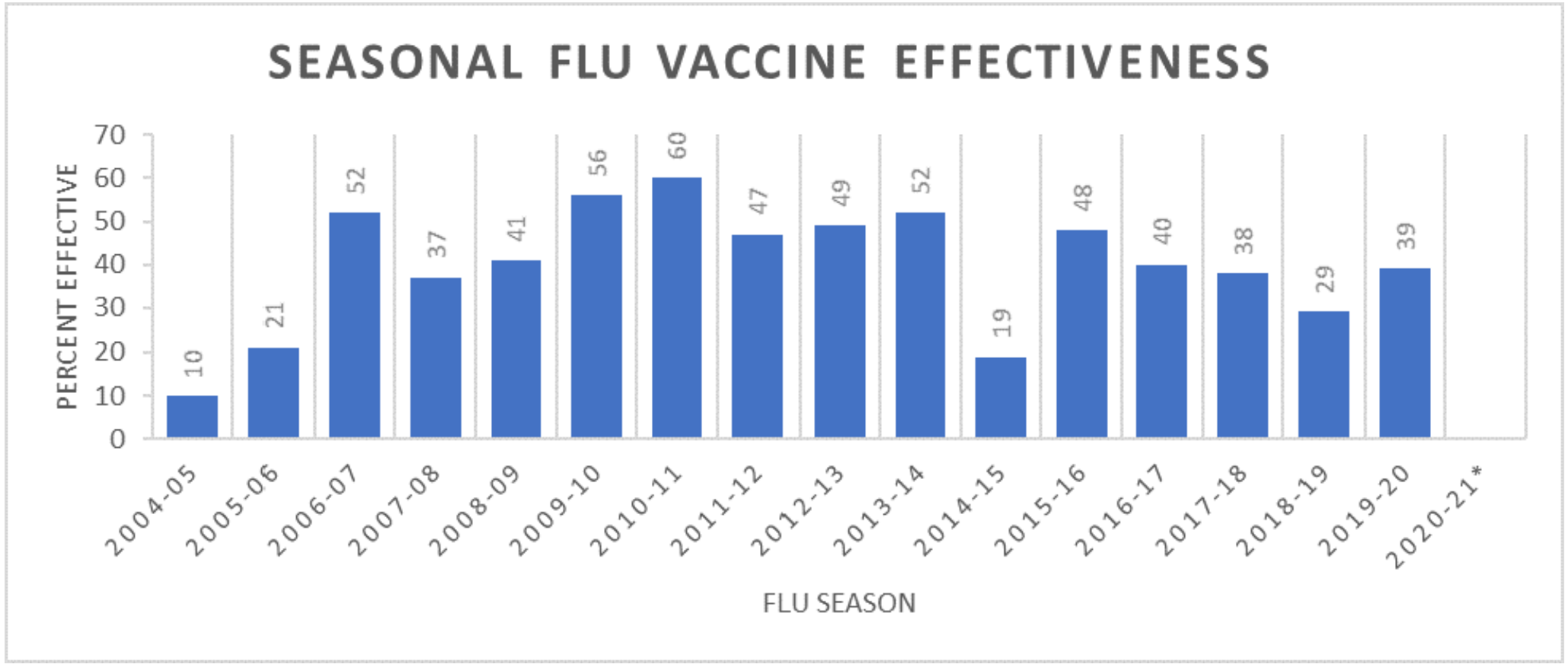
- individuals on immunosuppressive therapy, those with renal disease, and transplant recipients have impaired responses to vaccination. To be maximally effective, immunizations should be given before transplantation.

- The responsiveness to influenza vaccination in HIV-infected individuals is related to the degree of immunosuppression.

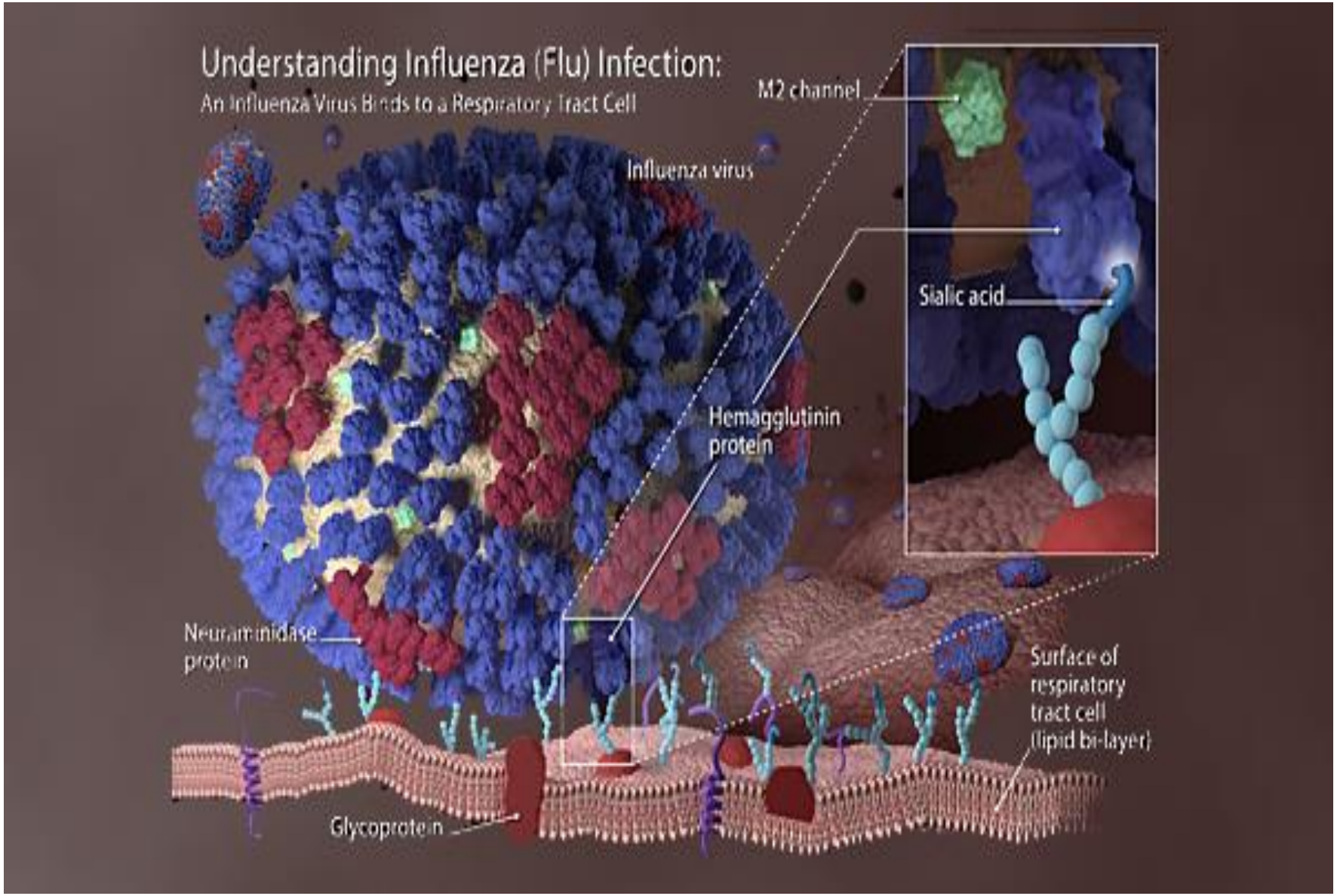
- A quadrivalent cell-based influenza shot :containing virus grown in cell culture, which is licensed for people 6 months and older. This vaccine is egg-free.
- Recombinant quadrivalent influenza shot : an egg-free vaccine, approved for people 18 years and older.
- A quadrivalent flu shot using an adjuvant (an ingredient that helps create a stronger immune response), approved for people 65 years of age and older.
- A quadrivalent high-dose influenza vaccine, which contains a higher dose of antigen to help create a stronger immune response, licensed for people 65 years and older.
- A live attenuated influenza vaccine , which is given intranasally. This vaccine is approved for people 2 through 49 years of age. Live attenuated influenza vaccine should not be given to people who are pregnant, immunocompromised persons, and some other groups.

- Inactivated and recombinant influenza vaccines may be administered concurrently or sequentially with other live or inactivated vaccines.

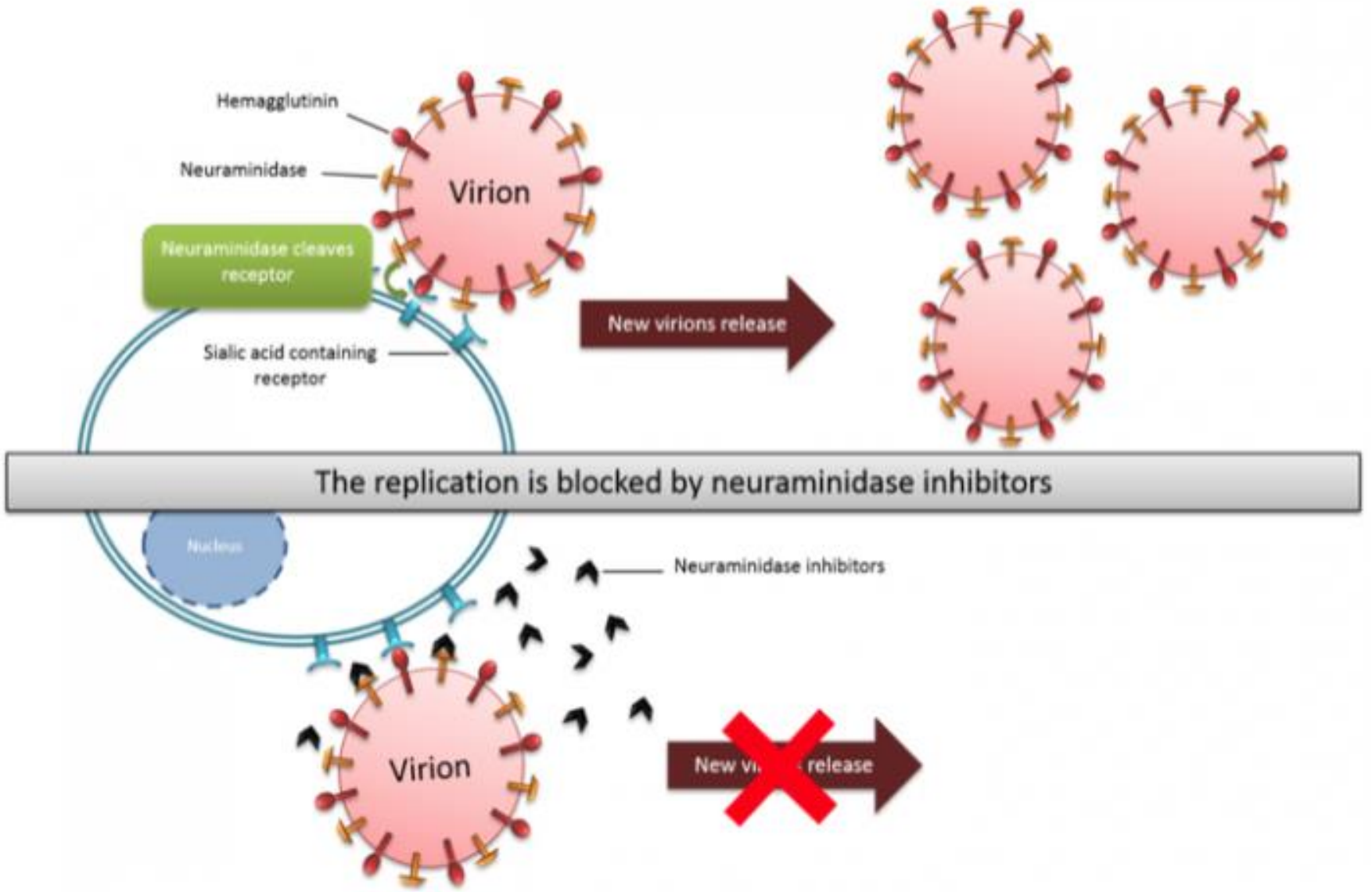
- Administration of inactivated influenza vaccine to persons receiving influenza antiviral drugs for treatment or chemoprophylaxis is acceptable.


SEASONAL FLU VACCINE EFFECTIVENESS
PERCENT EFFECTIVE
70
60
50
40
30
20
10
0
10
21
52
37
41
56
60
47
49
52
19
48
40
38
29
39
2004-05
2005-06
2006-07
2007-08
2008-09
2009-10
2010-11
2011-12
2012-13
2013-14
2014-15
2015-16
2016-17
2017-18
2018-19
2019-20
2020-21*
FLU SEASON

Treatment


Understanding Influenza (Flu) Infection:
An Influenza Virus Binds to a Respiratory Tract Cell
M2 channel
Influenza virus
Sialic acid
Hemagglutinin protein
Neuraminidase protein
Surface of respiratory tract cell (lipid bi-layer)
Glycoprotein

The action of neuraminidase in replication of virions in influenza infection.



	AMANTADINE[a]	RIMANTADINE[a]	ZANAMIVIR	OSELTAMIVIR	PERAMIVIR	BALOXAVIR
Protein target	M2	M2	Neuraminidase	Neuraminidase	Neuraminidase	Cap-dependent endonuclease
Activity	A only	A only	A and B	A and B	A and B	A and B
Side effects	CNS (13%) GI (3%)	GI (6%) GI (3%)	Bronchospasm	GI (9%)	GI (8%)	Diarrhea, bronchitis
Metabolism	None	Multiple (hepatic)	None	Hepatic	None	UGT1A3, CYP3A4
Excretion	Renal	Renal + others	Renal	Renal (tubular secretion)	Renal	Fecal (80%): urine (15%)
Drug interactions	Antihistamines, anticholinergics	None	None	Probenecid (increased levels of oseltamivir)	—	Antacids and laxatives reduce concentration
Dose adjustments needed	≥65 yr old CrCl <50 mL/min	≥65 yr old CrCl <10 mL/min	None	CrCl <30 mL/min Severe liver dysfunction	CrCl <30 mL/min	—
Contraindications	Acute-angle glaucoma	Severe liver dysfunction	Underlying airway disease			—
FDA-Approved Indications						
Therapy	Adults and children aged ≥1 yr	Adults only	Adults and children aged ≥7 yr	Adults and children aged ≥2 wk	Adults who cannot take oral or inhaled medications	Adults and children ≥12 yr of age[b]
Prophylaxis	Yes	Yes	Adults and children aged ≥5 yr	Adults and children aged ≥1 yr	—	—

M2 inhibitors

- Currently, all circulating influenza viruses are resistant to the M2
- inhibitors amantadine and rimantadine.
- Resistance is the result of single point mutations in the membrane-spanning region of the M2 protein, and it confers complete cross-resistance between amantadine and rimantadine.

Neuraminidase inhibitors

- NA may be important in facilitating the penetration of virus through secretions in the respiratory tract, which are rich in sialic acid–containing macromolecules.

- It removes the sialic acid from these cell surface glycoproteins. Destruction of these receptors by NA is critical in allowing newly formed viruses to subsequently egress from the cell and spread to other cells.

- Oseltamivir initiated within the first 36 hours of symptoms resulted in 30% to 40% reductions in the duration of symptoms and severity of illness and reduced rates of prolonged coughing.

- Endonuclease inhibitors interfere with viral RNA transcription and block virus replication in both influenza A and B viruses.

- Therapy is not necessarily universally indicated in all persons with influenza, but can be lifesaving in some persons(high risk of influenza complications).

- Resistance to antivirals has been observed frequently with almost all influenza antivirals, and the potential for generation of resistant viruses is an important component of therapy recommendations.

- In persons with severe illness or prolonged viral replication, even late therapy can occasionally be of benefit.