Influenza

Angelena M. Labella, MD[a,*], Susan E. Merel, MD[b]

KEYWORDS

• Influenza • Pandemic influenza • Viral illnesses • Immunization • Treatment
• Transmission • Chemoprophylaxis

KEY POINTS

- Clinicians should suspect influenza when a patient presents with respiratory symptoms, fever, and systemic symptoms and when influenza virus is circulating in the community.
- Rapid influenza diagnostic tests (RIDTs) can be helpful in confirming the diagnosis, but these are most helpful within 24 hours of symptom onset and have a higher positive predictive value when the prevalence of influenza in the community is high. Reverse transcriptase polymerase chain reaction (RT-PCR) has high sensitivity and specificity but may not be practical in all clinic settings.
- Treatment of influenza is most efficacious within 48 hours of the onset of symptoms. Patients with conditions that predispose them to high-risk complications of influenza and hospitalized patients should be treated regardless of the timing of onset of symptoms. In most cases, oral oseltamivir is the treatment of choice.
- Influenza vaccination is currently recommended for everyone older than 6 months in the United States. Trivalent vaccines are available in several formulations, including a live attenuated nasal spray and an inactivated vaccine in intramuscular and intradermal formulations. The effectiveness of the vaccine in preventing influenza is between 50% and 80% depending on the population; it can be worse in a year in which there is a poor match between vaccine and circulating influenza strains.
- During the 2009 influenza A/H1N1 pandemic, pregnant women and patients with morbid obesity were at high risk for complications including death.
- Although still rare, clinicians should be aware of emerging influenza strains including variant (v) H3N2, which generally requires swine exposure.

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[a] Section of Hospital Medicine, Division of General Medicine, Department of Medicine, New York Presbyterian, Columbia University Medical Center, 177 Fort Washington Avenue, New York, NY 10032, USA; [b] Hospital Medicine Program, Division of General Internal Medicine, Department of Medicine, University of Washington Medical Center, 1959 Northeast Pacific Street, Box 356429, Seattle, WA 98195-6429, USA
* Corresponding author.
E-mail address: aml2250@columbia.edu

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BIOLOGY AND GENETICS OF INFLUENZA

What Are the Different Types of Influenza?

The influenza virus is made up of 8 distinct RNA segments (**Table 1**).[1] These segments each code for a different protein that is essential to the structure and function of the virus. There are 3 genera of influenza viruses: A, B, and C.[2] Influenza A alone has caused pandemic illness, while influenza B and C have caused illness of epidemic proportion only.[3] Influenza A is further subtyped by the glycoproteins on its cell surface: hemagglutinin and neuraminidase. Hemagglutinin, for which there are 16 different molecules, allows the virion (a particle of virus) to anchor to a cell surface, while neuraminidase, for which there are 9 molecules, allows for digestion of host secretions and, later, release of viral particles from the host cell.[4] The influenza virus is named after the types of hemagglutinin and neuraminidase molecules.

How Does the Influenza Virus Change or Mutate Over Time?

Because the influenza virion is made up of 8 independent RNA strands it is subject to genetic changes. The 2 types of genetic changes that have been best described are antigenic drift and antigenic shift or reassortment. Reassortment is when 2 viruses infect the same host cell and then exchange genes during replication (**Fig. 1**). This process results in a new virion that has gene segments from each of its parent virus. This change occurs from viruses specific to one species and can also result in a new virus of interspecies origin. The H1N1 virus that caused the 1918 pandemic was derived from genes (or RNA segments) from human influenza, swine influenza, and avian influenza.[5] The influenza virus can also undergo smaller changes. RNA segments or genes mutate such that the hemagglutinin and neuraminidase molecule do not change their type but only some of their structure. In other words, they are still called by the same number (eg, H1, H2) but may not be recognized by the host's immune system as the same virus. This process is called antigenic drift.

Why Are These Changes Important and How Do They Affect Immunity?

Any antigenic change in the influenza virus, be small changes in the composition of the hemagglutinin molecule or a larger change such as interspecies reassortment, will decrease the likelihood of the host having effective immunity. In addition, the diversity in RNA composition of influenza viruses from year to year makes vaccine development

Table 1
Eight RNA segments of the influenza genome and corresponding protein and function

RNA Segment	Protein	Function
PB2	Transcriptase	Cap binding
PB1	Transcriptase	Cap elongation
PA	Transcriptase	Protease activity
HA	Hemagglutinin	Anchoring to cell
NP	Nuclear protein	RNA binding and transport
NA	Neuraminidase	Release of virus
M1/M2	Matrix proteins	M1, major component of virion; M2, ion channel
NS1/NS2	Nonstructural protein	NS1, RNA transports, translation; NS2, unknown function

Data from Morens DM, Taubenberger JK, Fauci AS. The persistent legacy of the 1918 influenza virus. N Engl J Med 2009;361(3):225–9.