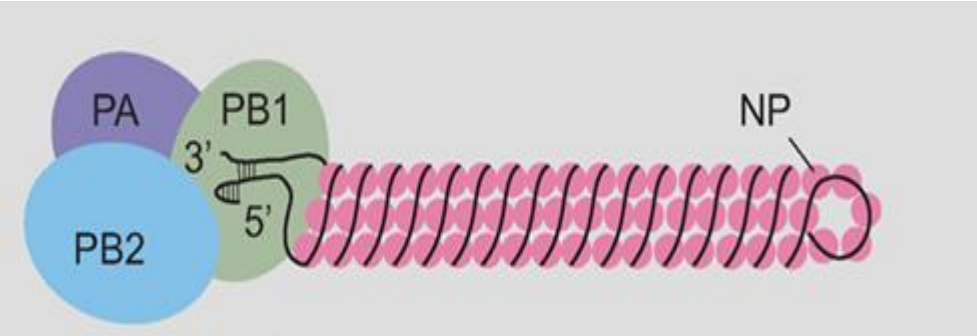
Medical Microbiology

Influenza-II

Dr. Dharmesh Harwani
Department of Microbiology

Cap Snatching



RdRp

- **PB1 first binds the 5' end of the viral RNA (vRNA), activating PB2 and causing the 3' end of the vRNA to form a double-stranded zone**
- **The PB2 proceeds to bind cellular mRNA at the N7-methyl guanosine (m^7G) capped 5' end.**
- **The PA subunit subsequently cleaves the sequence 10-15 nucleotides from the cap structure via endonuclease activity**
- **PB1 subunit contains the polymerase activity.**
- **The cap snatched primer moves the PB1 domain to serve as the primer for transcription.**
- **The viral 3' poly-A tail is added at the end of transcription and the resulting viral mRNA looks is identical to host mRNA, allowing endogenous cellular machinery to carry out processing and nuclear export.**

Epidemiology

- **Influenza spreads around the world in yearly outbreaks, resulting in about three to five million cases of severe illness and about 290,000 to 650,000 deaths**
- **Outbreaks occur mainly in the winter and Death occurs mostly in high risk groups.**
- **In the 20th century, three influenza pandemics occurred:**

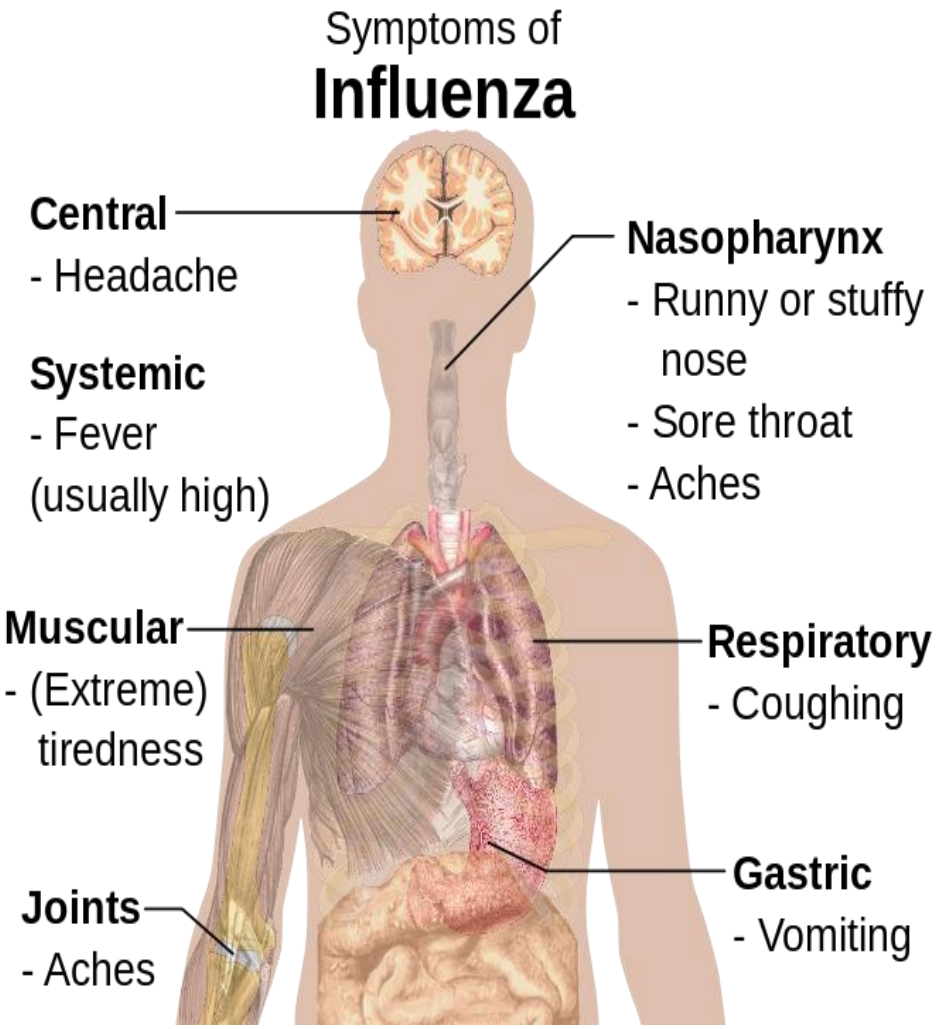
✓ Spanish influenza in 1918 (17–100 million deaths)

✓ Asian influenza in 1957 (two million deaths)

✓ Hong Kong influenza in 1968 (one million deaths).

- **The WHO declared an outbreak of a new type of influenza H1N1 to be a pandemic in June 2009.**

Symptoms

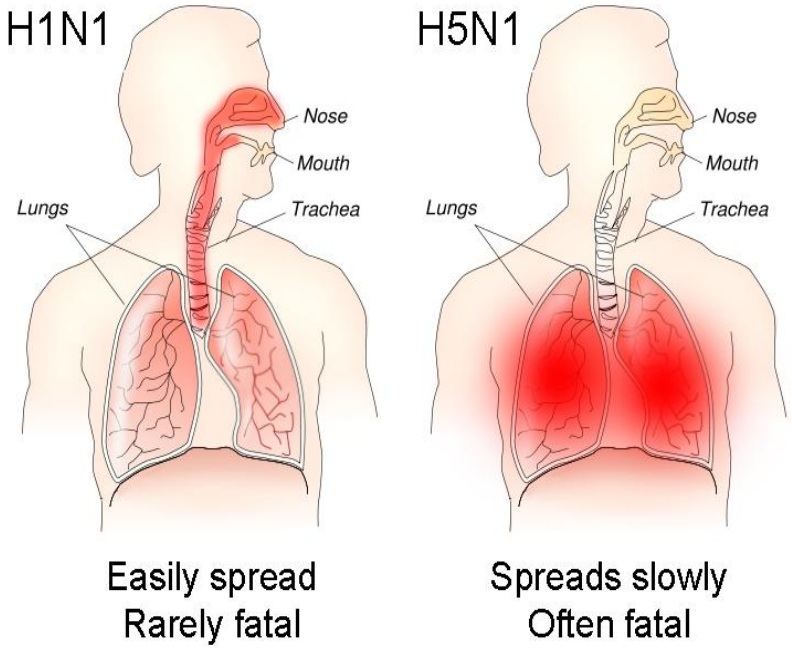


Approximately 33% of people with influenza are asymptomatic

Pathophysiology

- One of the mechanisms is believed to be the inhibition of adrenocorticotropic hormone (ACTH) resulting in lowered cortisol levels.

- In mild and avirulent viruses, the structure of the hemagglutinin means that it can only be cleaved by proteases found in the throat and lungs. Strains that are easily transmitted between people have hemagglutinin proteins that bind to receptors in the upper part of the respiratory tract.



- In contrast, the highly lethal H5N1 strain binds to receptors that are mostly found deep in the lungs.

- Common symptoms of the flu such as fever, headaches, and fatigue are the result of the huge amounts ofproinflammatory cytokines and chemokines (such as interferon or tumor necrosis factor) produced from influenza-infected cells.

Diagnosis

There are a number of rapid tests for the flu. One is called a **Rapid Molecular Assay**, when an upper respiratory tract specimen (mucus) is taken using a nasal swab or a nasopharyngeal swab.

Treatment

Medications such as acetaminophen (paracetamol) to relieve the fever and muscle aches associated with the flu. Since influenza is caused by a virus, antibiotics have no effect on the infection; unless prescribed for secondary infections such as bacterial pneumonia.

Antivirals

The two classes of antiviral medications used against influenza are neuraminidase inhibitors (oseltamivir, zanamivir, peramivir) and matrix protein inhibitors (adamantane).

These are the main ways that influenza spreads

•by direct transmission

•the airborne route

•through hand-to-eye, hand-to-nose, or hand-to-mouth transmission, either from contaminated surfaces or from direct personal contact such as a hand-shake.

- **When vaccines and antiviral medications are limited, non-pharmaceutical interventions are essential to reduce transmission and spread.**

- Strategies endorsed by experts for all phases of flu outbreaks include hand and respiratory hygiene, self-isolation by symptomatic individuals and the use of face masks by them and their caregivers, surface disinfection, social distancing including school closures and travel restrictions are recommended.

- **Researchers have estimated that such interventions during the 1918 Spanish flu pandemic in the US reduced the peak death rate by up to 50%, and the overall mortality by about 10–30%, in areas where multiple interventions were implemented.**

viruses

MDPI

Review

Insight into Influenza: A Virus Cap-Snatching

Corey De Vlugt †, Dorota Sikora † and Martin Pelchat *

Department of Biochemistry, Microbiology and Immunology, Faculty of Medicine, University of Ottawa, Ottawa, ON K1H 8M5, Canada; cdevlugt@outlook.com (C.D.V.); dorotasikora@yahoo.com (D.S.)
* Correspondence: mpelchat@uottawa.ca; Tel.: +1-613-562-5800 (ext. 8846)
† These authors contributed equally to this work.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6266781/pdf/viruses-10-00641.pdf

Low Plasma Levels of Adrenocorticotropic Hormone in Patients with Acute Influenza

William McK. Jefferies, James C. Turner, Monica Lobo, and Jack M. Gwaltney, Jr.

From the Departments of Internal Medicine and Student Health, University of Virginia Health Sciences Center, Charlottesville, Virginia

https://academic.oup.com/cid/article/26/3/708/289396