Influenza

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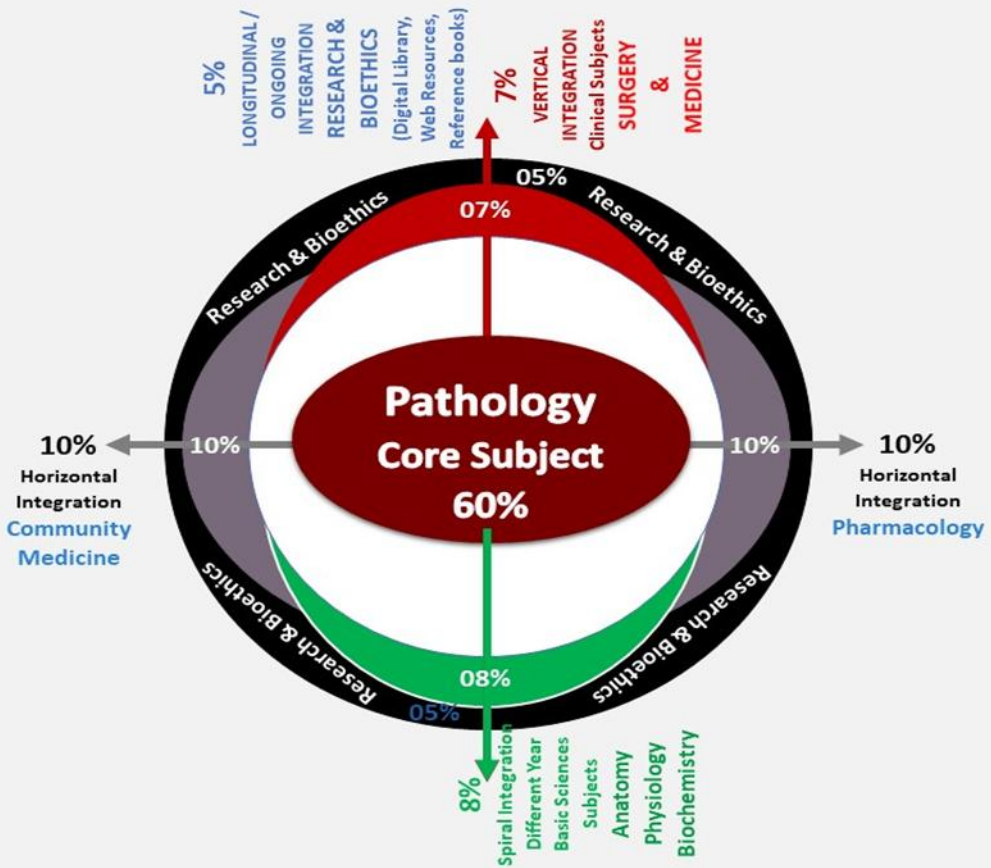
Prof. Umar, LGIS (Lecture) Model

Prof. Umar's Clinically Oriented Integration Model
For Basic Sciences Interactive Lectures



Model 3rd Year Pathology LGIS (≈30 slides)	
Core Subject – 60% (≈ 18-20 slides)	
Pathology (≈ 18-20 slides)	
Horizontal Integration – 20% (≈ 5-6 slides)	
Same Year Subjects	• Pharmacology (10%) (≈ 2-3 slides) • Community Medicine (10%) (≈ 2-3 slides)
Vertical Integration – 07% (≈ 2-3 slides)	
Clinical Subjects	• Medicine (3-5%) (≈ 1-2 slides) • Surgery (3-5%) (≈ 1-2 slides)
Spiral Integration – 08% (≈ 2-3 slides)	
Different Year Basic Sciences Subjects	• Anatomy (1-3%) (≈ 1-2 slides) • Physiology (1-3%) (≈ 1-2 slides) • Biochemistry (1-3%) (≈ 1-2 slides)
Longitudinal / Ongoing Integration – 05% (≈ 1-2 slides)	
Research & Bioethics (≈ 1-2 slides)	

RMU is thriving to upgrade the Integrated Clinical Oriented Modular Curriculum and Teaching. There are many deficiencies in this system which RMU has learned with five year experience of real ground experience. We have designed the teaching (lecture) model of integration, covering all components of vertical and horizontal and clinical integration along with continuous step ladder pattern of research, professionalism and ethic. This teaching strategy is in alignment with assessment principles of integrated modular curriculum.

LECTURE CONTENT ANALYSIS	
CORE SUBJECT	60%
VERTICAL INTEGRATION	20%
HORIZONTAL INTEGRATION	15%
RESEARCH	5%

LEARNING OBJECTIVES

At the end of this lecture students will be able to

- To understand the pathogenesis, route of transmission of the Influenza.
- To know the sign and symptoms, complications, and clinical management.
- To know about the measures used to prevent spread of influenza.

Introduction

- **Influenza**, also called **flu** or **grippe**, an acute viral infection of the upper or lower respiratory tract.
- Influenza is caused by any of several closely related viruses in the family Orthomyxoviridae (a group of RNA viruses).
- There are four types of influenza viruses: A, B, C and D.

Remember

Different types of Influenza virus generally produce similar symptoms but are completely unrelated antigenically, so that infection with one type confers no immunity against the others.

Introduction

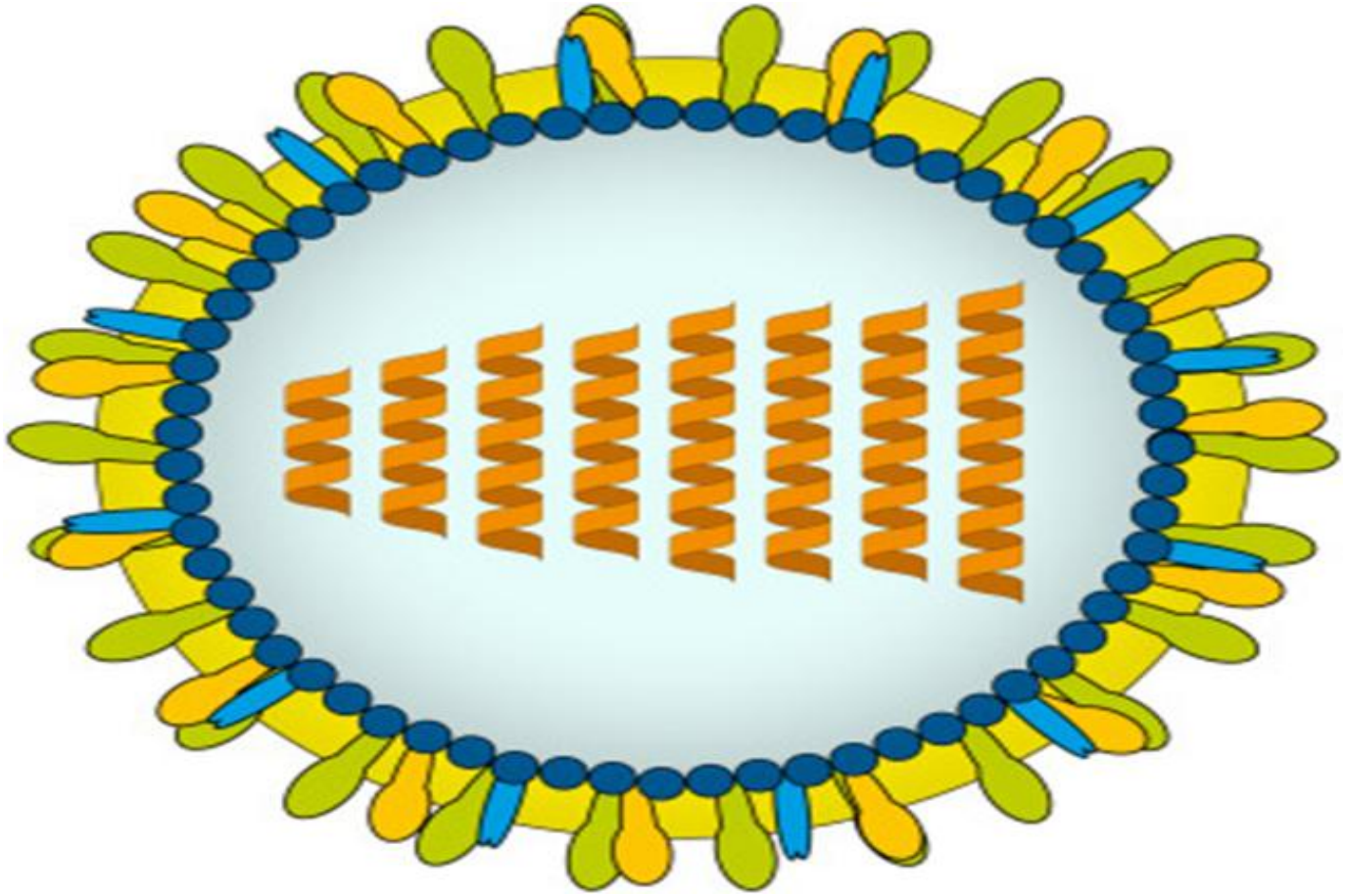
- Influenza A virus infects multiple species including humans, birds, swine, horses, seals, mink and whales with birds being the primary reservoir.
- Humans are the main reservoirs of Influenzas B and C.
- Cattle and pigs are the main reservoir of Influenza D.

Introduction

- The A viruses cause the great influenza **epidemics** and **pandemics**.
- B viruses cause smaller localized **outbreaks**.
- C viruses cause only mild respiratory illness in humans.
- Influenza D viruses are not known to infect humans and have been observed to cause disease only in pigs and cattle.

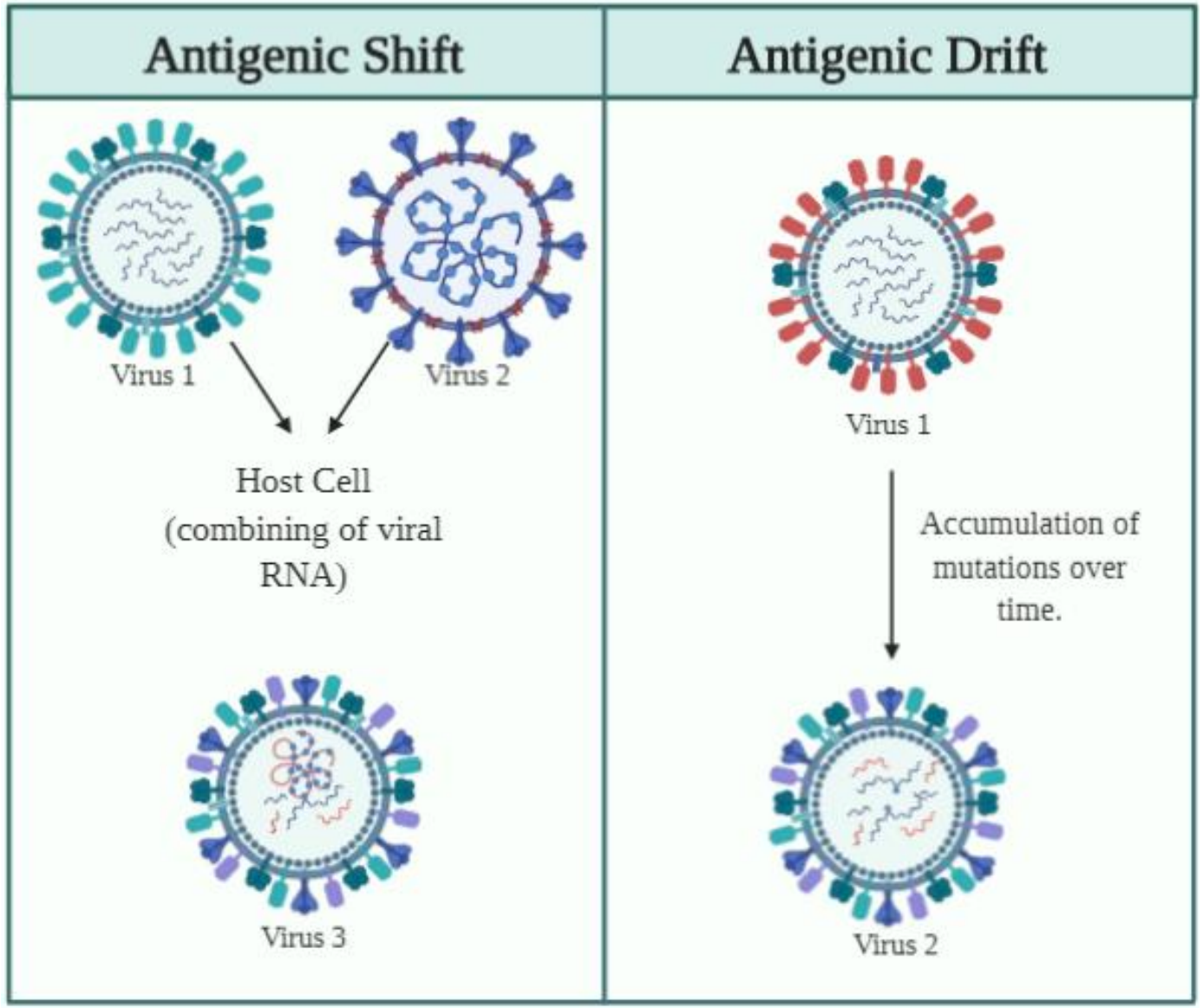
Influenza A

- Influenza A viruses are divided into subtypes based on two proteins on the surface of the virus: hemagglutinin (H) and neuraminidase (N).
- There are **18** different hemagglutinin subtypes and **11** different neuraminidase subtypes (H1 through H18 and N1 throughN11,respectively). Examples of influenza A subtypes include H1N1, H5N1, and H3N2.

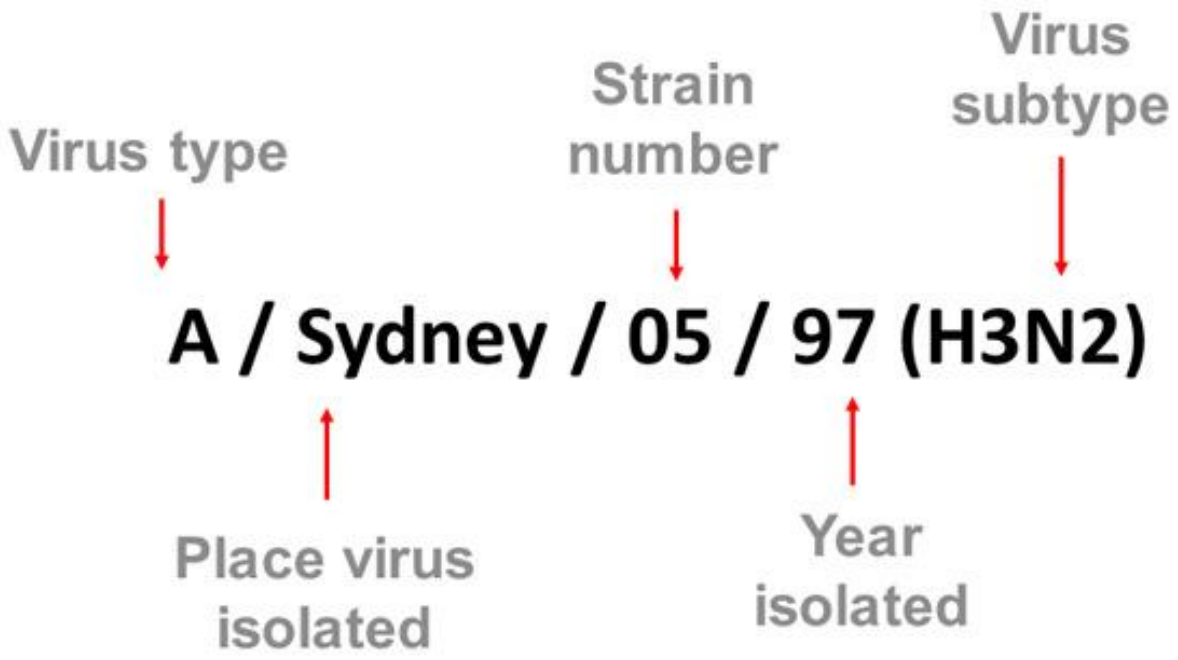


Influenza virus. Schematic representation of an influenza A virus (IAV). Hemagglutinin spikes (green) radiate all over the surface and are interspersed by neuraminidase (yellow) and matrix protein M2 (light blue). The latter are embedded in the envelope's lipid bilayer(light yellow), which in turn surrounds a layer of matrix protein M1 (dark blue). The segmented RNA (orange) of the virus is located in the interior.

- Hemagglutinin (HA) and neuraminidase (NA) are responsible for attachment, cell entry, and release of new particles.
- The NA and HA proteins are regularly subjected to small changes, which can produce viral strains causing annual epidemics. This phenomenon is called "antigenic drift."
- "Antigenic shift" is the process by which a sudden major change in the HA or NA proteins of IAV occurs due to genetic reassortment.


Antigenic Shift
Antigenic Drift
Virus 1
Virus 2
Host Cell
(combining of viral
RNA)
Virus 3
Virus 1
Accumulation of
mutations over
time.
Virus 2

Understanding the naming of flu viruses



- Pandemics occurred in 1918, 1957 and 1968 with the emergence of H1N1 Spanish influenza, H2N2 and H3N2 respectively, and most recently in 2009, with the emergence of H1N1 from swine (H1N1 2009pdm) into the human population.
- Influenza A virus was first isolated from throat washing of patient by Smith Andrews and Laidlaw in 1933.

Influenza B

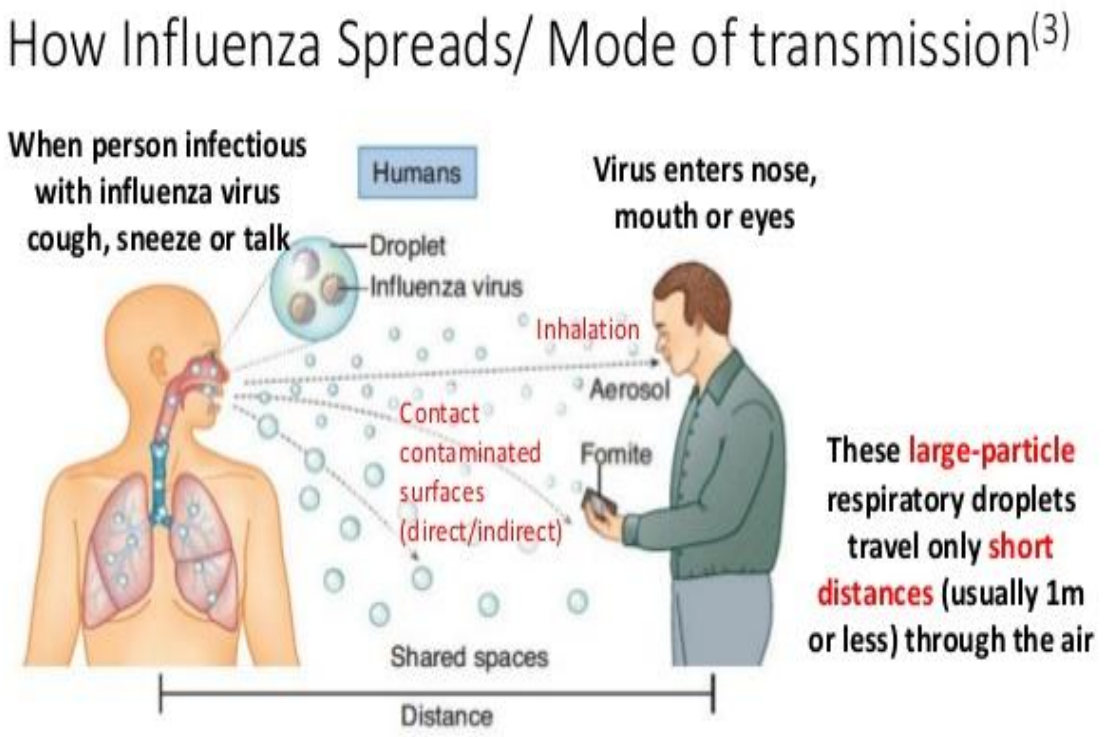
- Influenza B viruses are subdivided into two major lineages, B/Yamagata and B/Victoria.

Transmission

Droplet infection

Travel with cough and sneezing

Fomite transmission



Pathogenesis

The respiratory tract, upper and lower respiratory tract have sialic acid to which HA portion of virus bind.

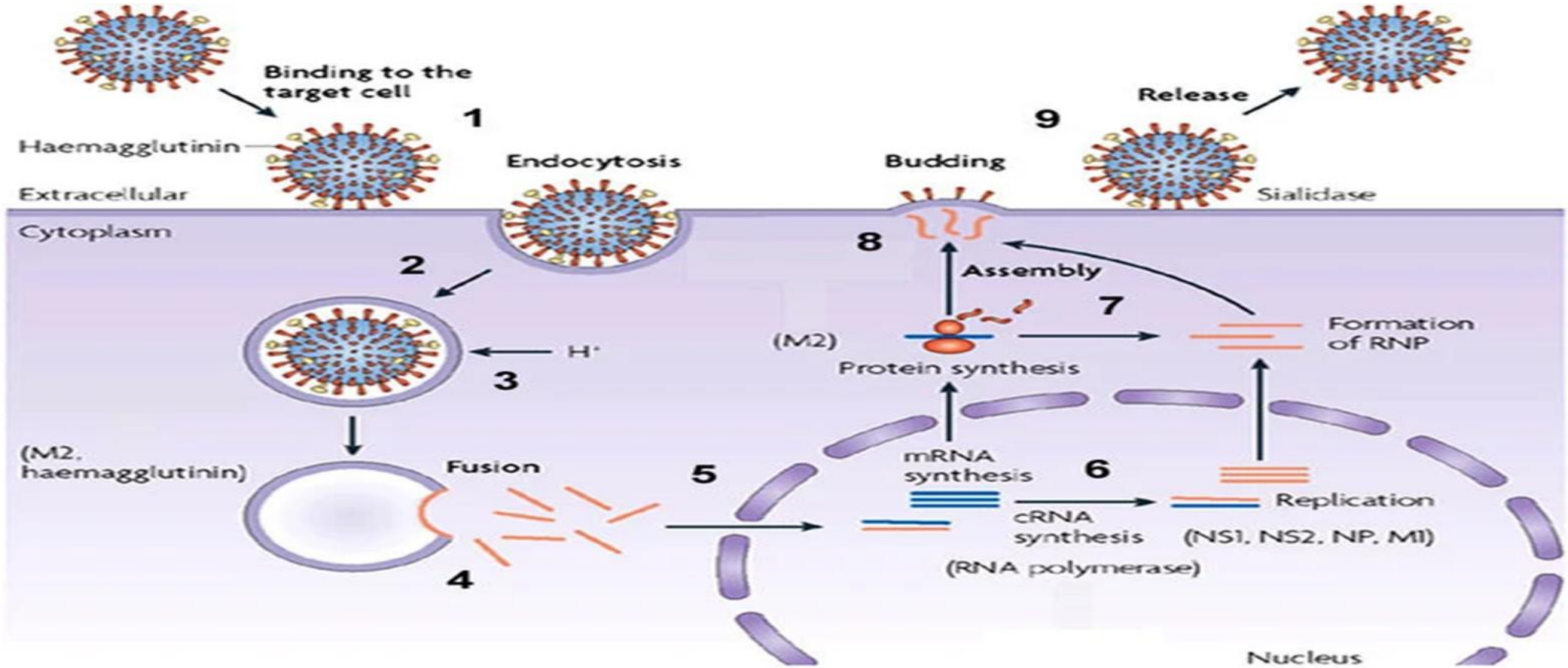
The replication of virus takes place in nucleus and progeny virions are soon produced and spread to adjacent cells.

Viral NA lowers the viscosity of the mucous film in the respiratory tract, laying bare the cellular surface receptors and promoting the spread of virus-containing fluid to lower portions of the tract.

Within a short time, many cells in the respiratory tract are infected and eventually killed.

The incubation period from exposure to virus and the onset of illness varies from 1 day to 4 days, depending on the size of the viral dose and the immune status of the host.

Viral shedding starts the day preceding onset of symptoms, peaks within 24 hours, remains elevated for 1–2 days, and then declines over the next 5 days.

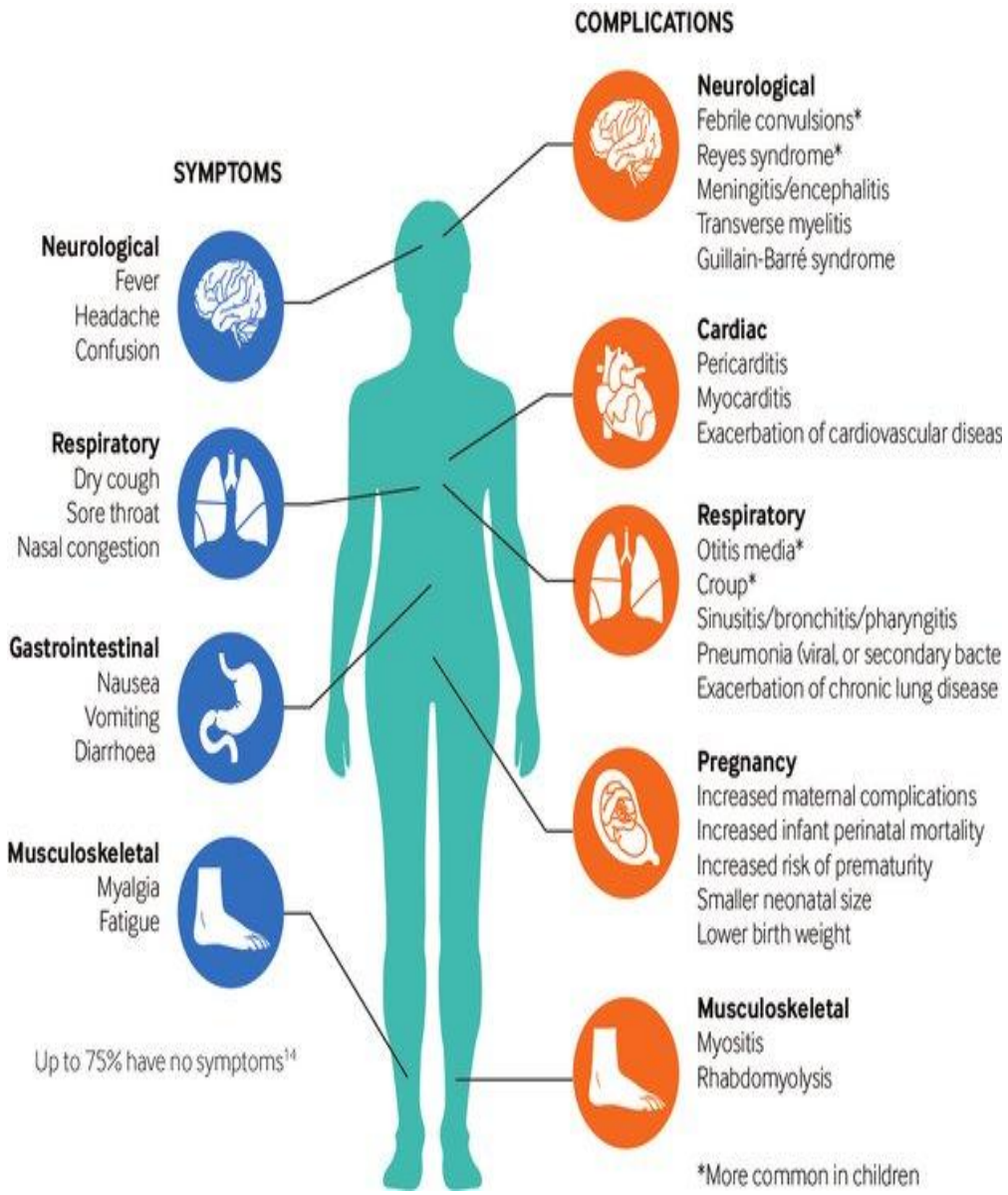

Binding to the target cell
1
Haemagglutinin
Extracellular
Endocytosis
Budding
9
Release
Sialidase
Cytoplasm
8
Assembly
2
7
(M2)
Formation of RNP
H+
3
Protein synthesis
(M2, haemagglutinin)
Fusion
5
mRNA synthesis
6
Replication
cRNA synthesis
(NS1, NS2, NP, M1)
(RNA polymerase)
4
Nucleus

Clinical manifestations

- Uncomplicated influenza illness is characterized by the abrupt onset of constitutional and respiratory signs and symptoms (e.g., fever, myalgia, headache, malaise, nonproductive cough, sore throat, and rhinitis).
- Uncomplicated influenza illness typically resolves after 3—7 days for the majority of persons, although cough and malaise can persist for >2 weeks.

Complications

- Tracheobronchitis and bronchiolitis
- Primary viral pneumonia
- Secondary bacterial pneumonia
- Myositis and myoglobinuria
- Reye's syndrome
- Viral Encephalitis and GBS



Laboratory findings and diagnosis

Rapid Influenza Diagnostic Tests

- Detects in minutes
- Vary in reliability
- Can detect type, not strain

Viral Cultures

- Grows virus

PCR

- Detects RNA

General management

Maintenance of fluid and electrolyte balance

Oxygen supplementation

Fever control with nonsteroidal anti-inflammatory drugs

Treatment of suspected secondary bacterial complications with antibiotics.

Isolation of patients

Anti- viral drugs

- Amantadine and Rimantadine are M2 ion channel inhibitors, thus preventing the pH changes that precede the membrane fusion step essential for nucleocapsid release.
- Zanamivir- potent inhibitor of neuraminidase and administered by inhalation.
- Oseltamivir- inhibitor of neuraminidase and administered orally.
- Baloxavir - inhibits the endonuclease activity of the polymerase protein, an influenza virus specific protein in the viral RNA polymerase complex required for viral gene transcription, resulting in inhibition of influenza virus replication.

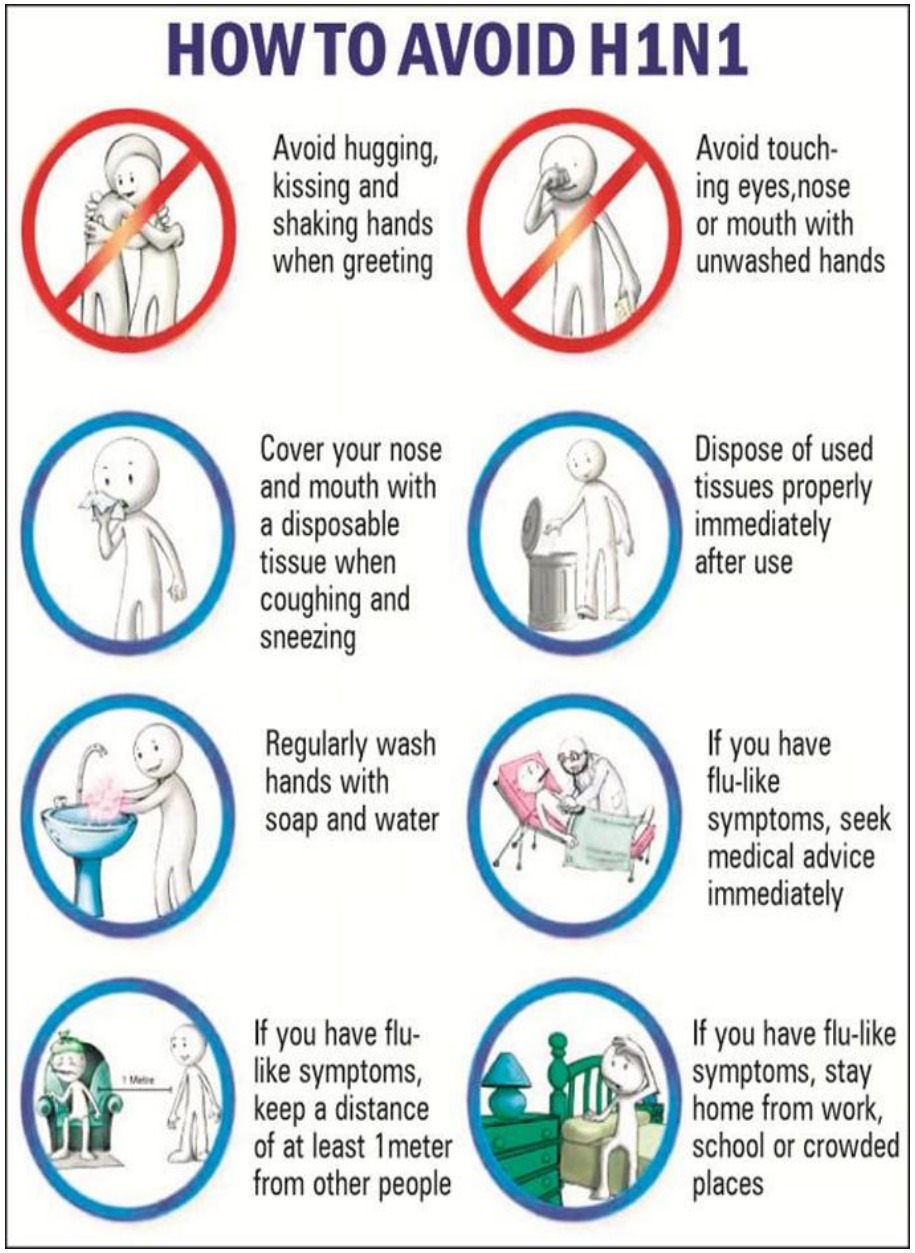
Prevention

What kills flu viruses?

Flu viruses are killed by heat above 167° F [75° C]. Common household

Cleaning products can also kill the flu virus, including products containing:

- chlorine
- hydrogen peroxide
- detergents (soap)
- iodophors (iodine-based antiseptics)
- alcohols



Vaccines

- **Trivalent inactivated influenza vaccine (TIV)/ Quadrivalent inactivated vaccines:** >6 months of age
- **Recombinant flu vaccines** : > 18 yrs.
- **Live attenuated influenza vaccine (LAIV)**: Nasal spray, 2 to 49 years
- Trivalent vaccines containing 3 strains(H1N1, H3N2, B Victoria lineage), Quadrivalent vaccines contain 4 strains(H1N1, H3N2, B Victoria, and B Yamagata)

- **Side Effects**: GBS, Allergic reactions
- Vaccines are not given to child less than 6 months of age
- Caregivers are vaccinated.
- Reduce risk of influenza by half
- Vaccine required every year

WHO SHOULD BE VACCINATED?

All children aged 6 through 59 months.

All persons aged ≥50 years.

Adults and children who have chronic pulmonary (including asthma), cardiovascular (excluding isolated hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus).

Persons who are immunocompromised due to any cause (including but not limited to immunosuppression caused by medications or HIV infection).

WHO SHOULD BE VACCINATED?

Women who are or will be pregnant during the influenza season.

Children and adolescents (aged 6 months through 18 years) who are receiving aspirin- or salicylate-containing medications and who might be at risk for experiencing Reye syndrome after influenza virus infection.

Residents of nursing homes and other long-term care facilities.

Persons who are extremely obese (body mass index ≥40 for adults).

Health care personnel, including all paid and unpaid persons working in health-care settings who have the potential for exposure to patients and/or to infectious materials.

Household contacts (including children) and caregivers of children aged ≤59 months (i.e., aged <5 years) and adults aged ≥50 years, particularly contacts of children aged <6 months; and

Household contacts (including children) and caregivers of persons with medical conditions that put them at higher risk for severe complications from influenza.

THE LANCET

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Influenza

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Summary

Summary

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