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Review article

Influenza and coronavirus zoonoses: an overview on pandemic events, viral genome, replication and emergency preparedness

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Abstract

Influenza and coronaviruses, zoonotic respiratory RNA viruses, cause global pandemics with major public health issues. These viruses exist as quasispecies due to the rapid evolution driven by their error-prone viral RNA polymerases and/or genomic organizations. They also show similar waves of infections/cases during the pandemic. However, there are some dissimilarities like severe disease in coronaviruses is due to cytokine-induced hyperactivity of the immune system, while secondary bacterial infection is a significant cause of death in influenza. Furthermore, unlike coronavirus, the segmented nature of influenza virus genome makes it easier for new strains to emerge through genetic reassortment, making its prevention and control more difficult. In this mini-review, we summarize the historical events of influenza and coronavirus pandemics or epidemics and the roles played by RNA viral genomes and pathogenesis in modulating viral evolution and generation of pandemic strains. Collectively, influenza and coronavirus diagnostics, vaccination, and other measures are critical for mitigating and controlling future pandemics. These pandemics might be regarded as a wake-up call to prepare us for future disasters.

Keywords: Influenza, Corona, SARS-CoV-2, Zoonotic, Pandemic, Pathogenesis

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Introduction

As the global human population grows, the demand for food and settlement space sharply increases, resulting in substantial ecological disturbances. Disturbed ecosystems are perfect environments for entry and sustenance of unknown and evolving pathogens with the potential to cause devastating impacts on both human and animal health. Changes in livestock and poultry feeding practices in recent years and the adverse climate and environmental changes have accelerated the prevalence and variation of pathogenic microorganisms, particularly viruses, and their ability to spread across species, thereby putting humans at greater risk of zoonotic diseases. So far, influenza and coronavirus pandemics are the most significant zoonotic events the world has seen in the last 100 years.

Both viruses have frequently crossed the species barrier, successfully adapted to humans, and caused significant epidemics and pandemics. Both influenza virus and coronavirus are RNA viruses with unpredictable evolution potential. The emergence of new strains which are genetically and antigenically distinct from circulating strains has accelerated the capabilities of these viruses to cross the species barrier and infect new hosts. It has also reduced the efficacy of the current preventive measures, particularly vaccines and antivirals. While the majority of human influenza epidemics and pandemics are caused by type A influenza viruses (H1N1 and H3N2 subtypes), avian influenza viruses subtypes H5N1, H5N6, H5N8, H7N9 and H9N2 have been responsible for several zoonotic infections (Widdowson et al., 2017). These strains originated from birds, especially waterfowl and land-based poultry (Abdelrahman et al., 2020). Swine influenza viruses have also been responsible for several zoonotic epidemics (Taubenberger and Morens, 2010) and the 2009 H1N1 pandemic (Neumann et al., 2009).

Coronavirus outbreaks and pandemics have emphasized the continued negative impacts of zoonotic diseases on human health and the global economy despite

the profound advancement of modern science. Most deadly infectious diseases originate from or are closely related to animals around us. The ongoing coronavirus disease 2019 (COVID-19) pandemic has caused over 514 million confirmed cases and over six million deaths worldwide (as of 8th May 2022) (WHO, 2022).

Comparative analysis of pandemic virus evolution patterns, host range, animal to human transmission, and processes by which they cross species barriers is critical in combating the current situation and preparing for future pandemics. Here, we describe the genomic and replication properties of viruses linked to distinct influenza and coronavirus pandemics.

Coronaviruses are known to cause major zoonotic diseases in the 21st century. Out of seven coronaviruses that are pathogenic to humans, three, namely, Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), Middle East Respiratory Syndrome Coronavirus (MERS-CoV-2), and the newly identified betacoronavirus SARS-CoV-2 have pandemic or epidemic potential (Manzanares-Meza and Medina-Contreras, 2020). SARS-CoV was first reported in China and 29 other countries and regions in 2003 (Ksiazek et al., 2003). In 2012, MERS-CoV spread through the Middle East, resulting in the MERS-CoV epidemic (Zumla et al., 2015). The ongoing COVID-19 pandemic caused by SARS-CoV-2 was first reported in Wuhan, China in 2019 (Chan et al., 2020). Bats are likely the natural reservoirs of human-infecting coronaviruses as all three epidemic/pandemic viruses are closely related to bat-origin coronaviruses (Chen, 2020). In various studies, the intermediate hosts of different coronaviruses are said to be civet cats (SARS-CoV), camels (MERS-CoV), and pangolin (SARS-CoV-2) (Raj et al., 2014; Wang et al., 2016; Zhang et al., 2020). A detailed history of influenza and coronavirus pandemics or epidemics, number of infected peoples, number of deaths, case fatality rate and their reproduction number are described in Table 1.

Pandemic or epidemic events

Influenza viruses and coronaviruses are respiratory viruses that cause pneumonia-like illnesses. These respiratory viruses have been a significant cause of pandemics and epidemics over the centuries. Like other zoonotic diseases, both influenza virus and coronavirus infections are of animal origin that spread by airborne transmission leading to rapid outbreaks.

In the first documented influenza pandemic commonly known as the "Spanish flu", about 500 million people, one-third of the human population at that time, were infected, and 50 million deaths were recorded over two years. The Spanish flu" was initiated by an avian-origin H1N1 strain of influenza A virus which occurred in four waves from 1918 to 1920 (Bassareo et al., 2020). However, another influenza pandemic is thought to have happened in 1889-90 in Russia and was likely caused by H3N8 and H2N2 strains (Ryan, 2008). Two more flu pandemics referred to as "Asian flu" and "Hong Kong flu", were experienced in 1957 and 1968. The H2N2 and H1N1 viruses involved in these pandemics had reassortant genomes comprising human and avian-origin gene segments (CDC, 2019; Martini et al., 2019).

The latest influenza pandemic, known as "Swine flu", was caused by a novel H1N1pdm09 virus in 2009 (Riley et al., 2011; Dawood et al., 2012). H1N1pdm09 virus resulted from triple reassortment between avian, swine, and human influenza viruses (Tewawong et al., 2015). The various pandemic and epidemic events of influenza and coronaviruses and their host relationships are illustrated in Figure 1.

Genome organization

While the genomes of influenza viruses and coronaviruses exist as single-stranded RNA molecules encapsulated by nucleoprotein, they differ in polarity and segmentation. Influenza A virus is an orthomyxovirus with 8 negative-sense RNA gene segments, whereas SARS-CoV-2 is a *Betacoronavirus* with a non-segmented, positive-sense RNA genome (Brian and Baric, 2005; Dadonaite et al., 2019). The eight segments of the influenza virus are named according to the major proteins they encode: two surface glycoprotein Hemagglutinin (HA) and Neuraminidase (NA), Polymerase basic 1 and 2 (PB1 & PB2) subunits, Polymerase acidic (PA) subunit, Nucleoprotein (NP), Nonstructural proteins (NS) and Matrix proteins (M) (Dadonaite et al., 2019) (Figure 2A).

On the other hand, the non-segmented coronavirus genome has ORFs for a polymerase complex (ORF1a and ORF1b), structural protein like Spike (S) gene, Envelope (E) gene, Membrane (M) gene, Nucleocapsid (N) gene, and several proteins whose functions are yet to be demonstrated (Zhu et al., 2020). The S protein of coronaviruses is a trimeric glycoprotein that contains two subunits (S1 and S2) that mediates the replication process (Burkard et al., 2014) (Figure 2B).

Replication and pathogenesis of influenza virus

Influenza virus enters the host cell via receptor-mediated endocytosis, where the acidic environment within the endosome induces conformational changes of the HA molecule to trigger the fusion of the viral and endocytic membranes resulting in the release of viral ribonucleoproteins (vRNPs) into the cytoplasm (Dadonaite et al., 2019). When these vRNPs are actively transferred from the cytoplasm to the nucleus through nuclear pores (Shaw and Palese, 2013), they act as a transcription template (Figure 3A). Transcriptase including PB1, PB2, and PA converts this negative-sense viral RNAs to positive sense messenger RNAs (mRNAs) to produce viral proteins. After that, new vRNPs are formed when NP and RNA polymerase components interact with newly generated viral RNA (Nordholm et al., 2017; Dou et al., 2018). The new vRNPs are then exported from the nucleus into the cytoplasm, eventually reaching the cell membrane where new virus particles are formed. The matrix protein (M1) and the nuclear export protein (NEP/NS2) are two viral proteins that control the nuclear export of RNPs from outside the host (Pflug et al., 2017).

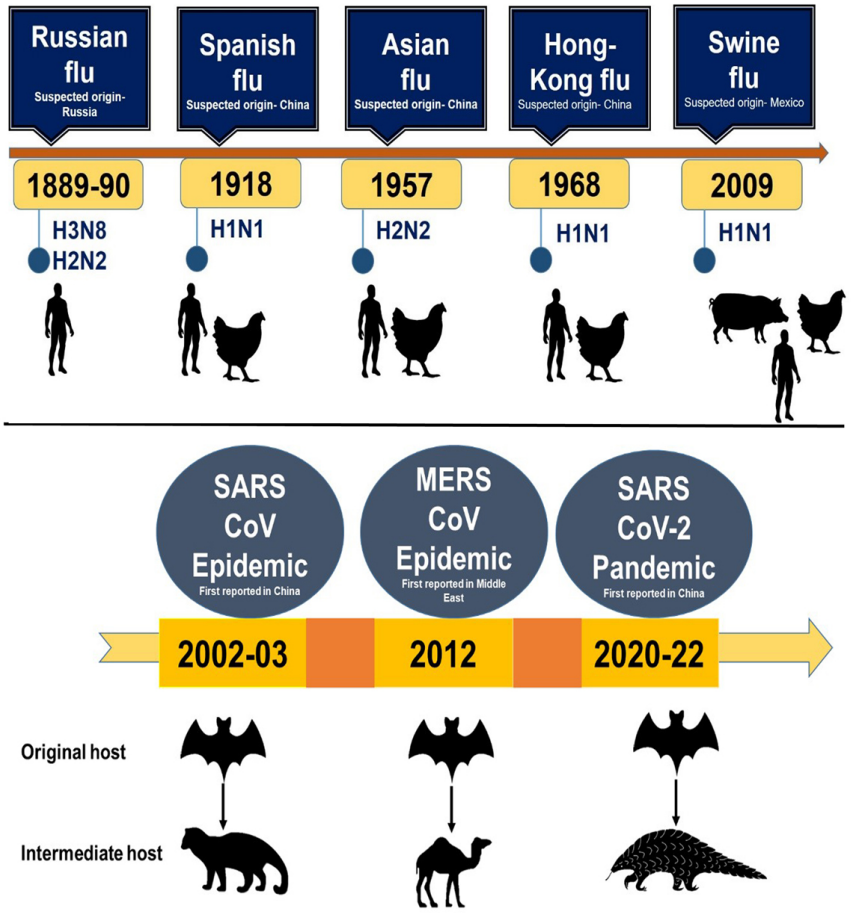

Figure 1: Pandemic and epidemic events of influenza (upper panel) and coronavirus (lower panel) showing the year of outbreak, host interactions and strains.

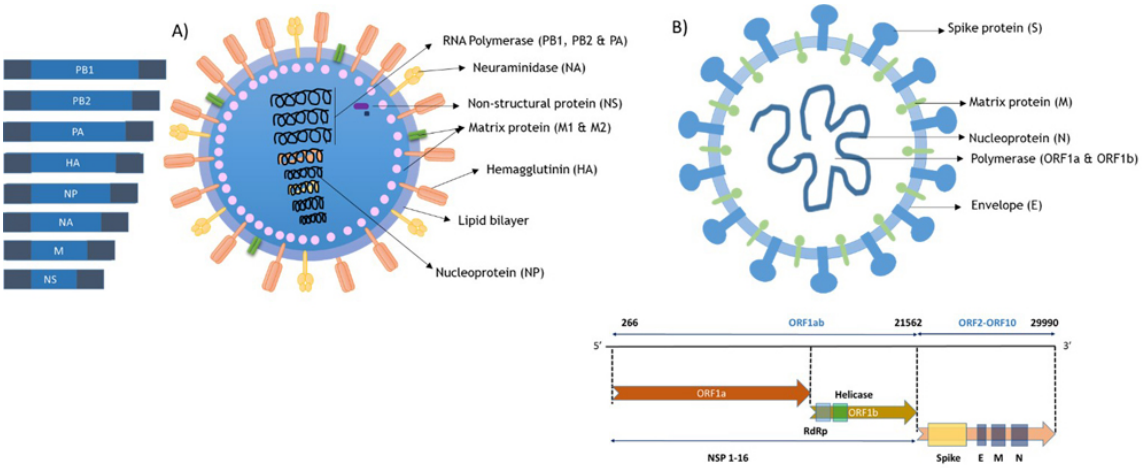

Figure 2: Genome organization of influenza virus (A) and coronavirus (B).

Table 1: History of influenza and coronavirus pandemics.

Pandemic name	Year of outbreak	Strain	Suspected origin country and intermediate host	Approximate number of infected people	Approximate number of deaths	Case fatality rate	Reproduction number
Russian flu	1889-1890	H3N8, H2N2	Russia (Human)	300–900 million	1 million (Valleron et al., 2010)	0.1-0.28 (Valleron et al., 2010)	2.1 (Valleron et al., 2010)
Spanish flu	1918–1920	H1N1	China (human, chicken)	>1 billion (Martini et al., 2019)	40–50 million (Barro et al., 2020; Kessler et al., 2021)	2-3% (Martini et al., 2019)	1.2-3.0 (Vynnycky et al., 2007)
Asian flu	1957–1958	H2N2	China (human, chicken)	>500 million[a]	1.5–2 million[a]	¡0.6%	1.53–1.70 (Biggerstaff et al., 2014)
Hong Kong flu	1968–1970	H3N2	China (human, chicken)	>500 million[a]	1–2 million[a]	<0.2%	1.56–1.85 (Biggerstaff et al., 2014)
Swine flu	2009–2010	H1N1	Mexico (swine, avian, human)	0.7 to 1.4 billion (Kelly et al., 2011)	Up to 575,000 (Dawood et al., 2012)	0.01% (Riley et al., 2011)	1.30–1.70 (Biggerstaff et al., 2014)
SARS-CoV	2002-2003	-	China (rabid cat, bat, civet)	8096 (Cherry, 2004)	774 (Cherry, 2004)	9.6% (Park, 2020)	2-5 (Chen, 2020)
MERS-CoV	2012-present	-	Saudi Arabia (camel)	2589[b]	893[b]	34.5%[b]	<1 (Chen, 2020)
SARS-CoV 2[c]	2019-present	Variants	China (unknown)	532 million	6.3 million	1.24%	3.1 (initial stage)

[a] Available online at: https://www.sinobiological.com/research/virus/1968-influenza-pandemic-hong-kong-flu.

[b] Available online, accessed on July 3, 2022) at : http://www.emro.who.int/health-topics/mers-cov/mers-outbreaks.html.

[c] As of 31st May 2022.

The human seasonal H1 and H3 virus subtypes HA proteins mainly recognize receptors with terminal α-2,6 sialic acid moieties, primarily found on bronchial epithelial cells of the human upper respiratory tract (URT) (Johnson and Mueller, 2002; Molinari et al., 2007). Different viral proteins act as virulence factors, such as viral protein PB1 induces apoptosis, promotes bacterial growth, and acts as an interferon antagonist. In addition, NA promotes the efficient release of viral progeny from the cell (Marcus et al., 2005), and NS1 and polymerase complexes are multifactorial interferon antagonists (Marcus et al., 2005; García-Sastre, 2011).

Influenza viruses usually cause mild to moderate upper respiratory tract illness. Infection of the lower respiratory tract of humans can result in pneumonia with progression to acute respiratory distress syndrome (ARDS), secondary bacterial infection, and death from respiratory failure. Influenza-mediated damage to the alveolar epithelium results from intrinsic viral pathogenicity due to its tropism to alveolar epithelial cells and host factors (Peteranderl et al., 2016).

Replication and pathogenesis of coronavirus

Despite the large number of investigations being undertaken since the beginning of the COVID-19 pandemic, the pathogenesis of SARS-CoV-2 and other SARS coronavirus is still unclear. It is known that coronavirus binds to the Angiotensin Converting Enzyme 2 (ACE2) receptor of the host cell (Cevik et al., 2020), and enhanced binding affinity between SARS-CoV-2 and ACE2 has been proposed to correlate with elevated virus transmissibility and disease severity in humans (Walls et al., 2020; Wan et al., 2020). Although the ACE2 receptors are greatly present in lung epithelial cells, their presence in other different tissues such as the intestine and endothelial cells in the kidney and blood vessels may lead to gastrointestinal and cardiovascular complications in the host (Monteil et al., 2020).

The infection occurrence pattern also depends on the structure of SARS-CoV. The surface spike protein is reported to assist the viral entry and binding to the ACE2 receptor, where envelope protein maintains the assembly (Song et al., 2019). Binding to the receptor is followed by activation of the spike protein through proteolytic cleavage by a host protease near the junction between its S1 and S2 domains (Millet and Whittaker, 2015; Hoffmann et al., 2018). Insertion of the newly liberated S2 domain N-terminus into the cell membrane leads to fusion of the viral and cellular membranes, resulting in the transfer of the viral RNA into the host cell cytoplasm, where viral replication can occur (Figure 3B).

The RNA genome is released into the cytosol by endocytosis, where it is translated into the replicase proteins (ORF1a/b). A virus-encoded protease splits the polyproteins (pp1a and pp1b) into individual replicase complex nonstructural proteins (nsps) (including the RNA-dependent RNA polymerase: RdRp). In the endoplasmic reticulum (ER)-derived double-membrane vesicles (DMVs), which eventually assemble to create complex webs of convoluted membranes, viruses initiate replication. Here, full-length negative-strand RNA and subgenomic (sg)RNA are produced using the incoming positive-strand genome as a template. Both structural and nonstructural proteins (referred to here as N, S, M, and E) are produced by sgRNA translation (Snijder et al., 2006; Perlman and Netland, 2009; Wu and Brian, 2010; Lu et al., 2020).

Like influenza viruses, coronaviruses produce pathologic lesions in the lung, heart, kidney, and liver where SARS-CoV 2 causes additional mild damage to the olfactory epithelium, dysfunction, and loss of taste and smell (Cevik et al., 2020; Sia et al., 2020). Pathogenesis of SARS-CoV consists of four phases, including 1) viral replication, 2) immune hyperactivity, 3) pulmonary destruction, and 4) clinical phases (viremia, acute, and recovery) (Lin et al., 2020). Other studies have described similar phases of pathogenesis, including viral invasion and replication, dysregulated immune response, multiple organ damage, and recovery (Navas-Martín and Weiss, 2004; Millet and Whittaker, 2015; van den Brand et al., 2015; Skariyachan et al., 2019; Li et al., 2020).

Transmission and clinical features

Both influenza (flu) and COVID-19 spread mainly among people who are in close contact with each other. In addition, the virus can spread from an infected person's mouth or nose in small liquid particles when they cough, sneeze, speak, sing or breathe. In the case of flu and COVID-19 infectivity, short-range aerosol or short-range airborne and droplet transmission are also common (WHO, 2020, 2021).

Generally, influenza symptom includes headache, myalgia, malaise, anorexia, sore throat, nonproductive cough, sneezing, and nasal discharge (Nicholson, 1992). Uncomplicated influenza illness is typically characterized by the abrupt onset of constitutional and upper respiratory tract signs and symptoms. Atypical signs and symptoms and asymptomatic influenza virus infection can also occur (CDC, 2020a).

COVID-19 symptomatic patients commonly present with high fever, cough, and shortness of breath and less commonly with a sore throat, anosmia, dysgeusia, anorexia, nausea, malaise, myalgias, and diarrhea (Stokes et al., 2020; Cascella et al., 2022). If an older person has secondary health concerns, complications may result in hospitalization. Unvaccinated patients have a higher risk of developing a critical or deadly illness while hospitalized, and COVID-19 has a higher in-hospital fatality rate than influenza (Cates et al., 2020).

Diagnosis

Diagnostic tests available for influenza include viral culture, serology, rapid antigen testing, reverse transcription polymerase chain reaction (RT-PCR), immunofluorescence assays, and rapid molecular assays (CDC, 2022b). The diagnosis of SARS-CoV-2 infection is often confused with influenza and seasonal upper respiratory tract viral infections (Kevadiya et al., 2021). However, the line of diagnosis is almost similar

Table 2: Differences in influenza and coronavirus pathogenesis, diagnosis, treatment, and vaccination at a glance.

Parameters	Sections	Influenza*	COVID-19*
Transmission	Route	Droplet, aerosol and contact	Droplet, aerosol, contact, fecal-oral route, and urethral route
	Reproduction number (R0)	R0 of several influenza pandemics is 1.46	Ro= 2.2-2.6
	Case fatality rate (CRF)	Children are the most susceptible population to catching influenza, with <1%	More severe in old ages with a CFR of 1.20%
Viral entry	Surface protein	Hemagglutinin protein helps the virus to bind to the host cell	The virus binds to the host cell with the help of spike protein
	Receptor	Human influenza: α-2,6-linked sialic acid Avian influenza: α-2,3-linked sialic acid	Spike protein binds to the receptor Angiotensin-Converting Enzyme 2 (ACE2) present in the host cell
	Endocytosis	Active endocytosis occurs in the host cell	No endocytosis occurs during entry to the host cell
Virus replication	Mechanism	Firstly, the fusion of virus and endocytic membrane, thus release of vRNP which mainly act as a template and finally converted to mRNA and exported to cytoplasm from nuclease with the help of transcriptase of PB1, PB2, and PA	Alveolar macrophage (M1) assists in replication in the host cell
	Virus release	M1, NEP/NS2 proteins responsible to expel the virus	Envelope protein mainly expel the virus from the host cell
Clinical features		Fever Chills Respiratory symptoms	Fever Respiratory symptoms Typical diffuse alveolar damage Diarrhoea
Diagnosis		Rapid antigen test	Rapid antigen test
		Molecular test likely RT-qPCR Virus culture	Molecular test likely RT-qPCR Virus culture
Vaccination	Target structure	Whole virus, Haemagglutinine	Spike Protein
	Technology	Live attenuated, inactivated, recombinant	mRNA-based, vector based, inactivated
	Mode of administration	IM, nasal spray	IM
	Modification according to the current strain	Modified twice a year	Still not modified, but genomic surveillance running
Treatment	Antivirals	Oseltamivir (Tamiflu®) Zanamivir (Relenza®) Peramivir (Rapivab®)	Nirmatrelvir with ritonavir (Paxlovid) Remdesivir (Veklury) Molnupiravir (Lagevrio)
	Monoclonal antibodies (MAb)	MAb CR6261 MAb CR8020	Bebtelovimab Tocilizumab, Bariticib
	Convalescent plasma	Not commonly used	Used in COVID-19

* The source of information is based on the references cited in the respective text.

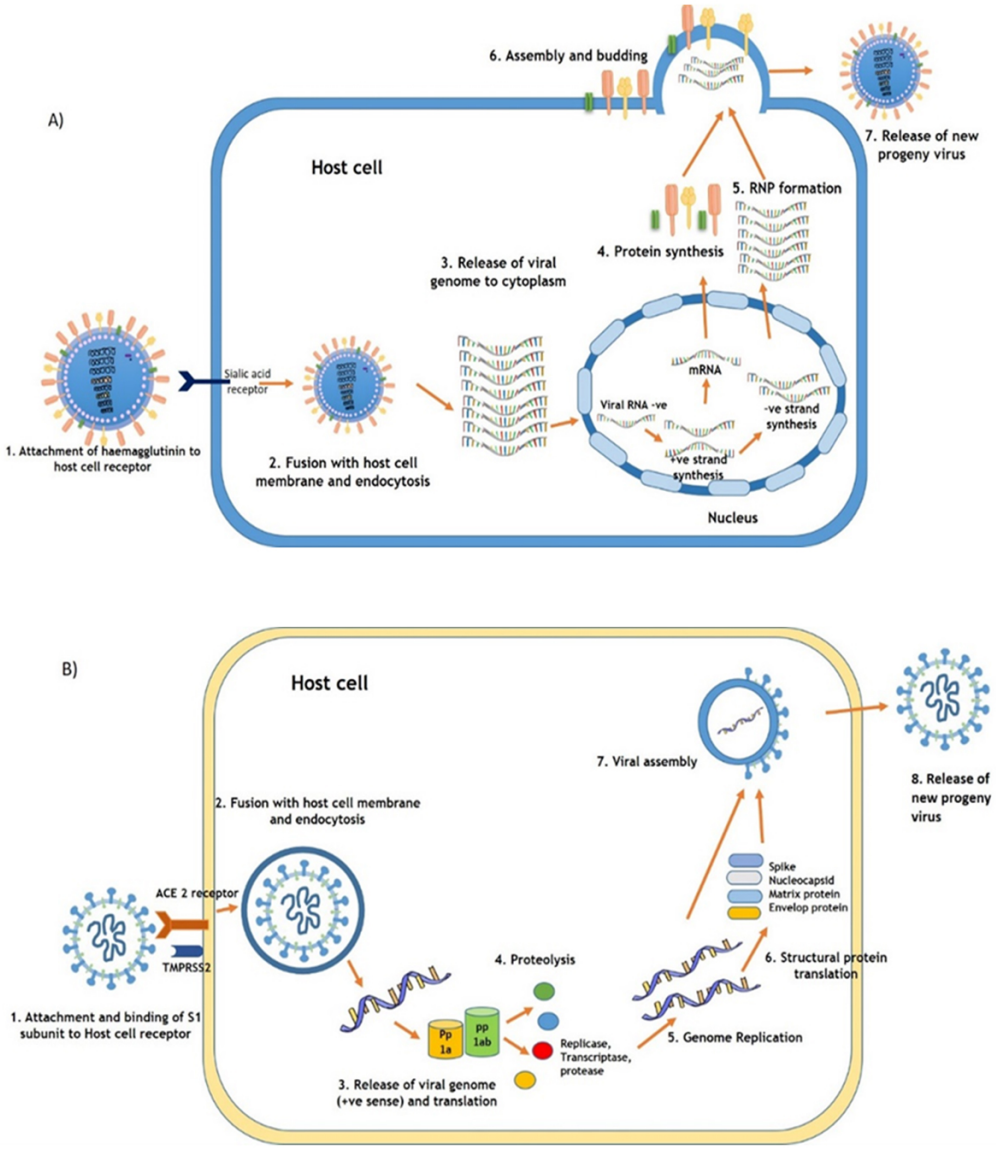

Figure 3: Graphical representation on replication of influenza and coronavirus. A) Influenza virus entry, replication mechanism in host cell cytoplasm and nucleus followed by viral release are shown . B) Coronavirus attachment, fusion, replication assembly within host cell cytoplasm and viral release are illustrated.

to influenza. Rapid and accurate COVID-19 and influenza detection is crucial for controlling outbreaks in the community and hospitals (To et al., 2020).

Nasopharyngeal and oropharyngeal swabs, nasal washes, and expectorated are standard diagnostic samples for COVID-19 and influenza infection (Donaldson et al., 1978; CDC, 2020b). Besides RT-PCR or RT-qPCR, other molecular techniques such as reverse transcription loop-mediated isothermal amplification (RT-LAMP) are current coronavirus diagnostic tests widely used worldwide (CDC, 2020b). RT-LAMP has a similar sensitivity to RT-qPCR, is highly specific, and is used to detect MERS-CoV (Lee et al., 2016; Huang et al., 2018). Serology testing is currently not widely available for COVID-19. In the case of human influenza, a presumptive diagnosis can be made by a validated rapid antigen or "point-of-care" test (Dwyer et al., 2006). To confirm a recent infection, serology is used to detect the antibody level in acute and convalescent serum samples.

Treatment

Treatment of flu and COVID-19 is mainly based on presenting symptoms such as pneumonia. Antiviral drugs and monoclonal antibodies (MAbs) are the two main lines of treatment applied for many years to treat viral diseases (Richman and Nathanson, 2016). Antiviral medicines target specific parts of the virus to stop it from replicating in the body and help to prevent being hospitalized or dying from the disease. Medications to treat either COVID-19 or influenza must be prescribed by a healthcare provider and started immediately after diagnosis to be effective. Taking antiviral drugs early is especially important for people at high risk for flu or COVID-19 complications, such as the elderly or people with compromised immune systems (NIH, 2017; CDC, 2022a).

Influenza pandemics and seasonal outbreaks cause millions of severe cases and deaths of approximately half a million people yearly (NIH, 2022). However, most people with the mild disease do not require medical attention or antiviral medication. Currently, there are three antiviral drugs recommended for treating the flu: oseltamivir (Tamiflu®), zanamivir (Relenza®), and peramivir (Rapivab®). As an empirical treatment, oseltamivir, a neuraminidase blocker that interferes with the virus's release from the host cell, can be used orally. According to the Centers for Disease Control and Prevention (CDC) guidelines for the 2021-2022 influenza outbreak, outpatients with suspected or confirmed uncomplicated influenza can be treated with oral oseltamivir, inhaled zanamivir, intravenous peramivir, or oral baloxavir depending upon age groups and contraindications (CDC, 2022b; NIH, 2022).

Similar to the influenza virus, asymptomatic and mild coronavirus diseases are usually self-limiting. But, people with co-morbidities, older people, and unvaccinated people should be monitored closely for symptoms. The three primary CDC-recommended antivirals medicine for COVID-19 are nirmatrelvir with ritonavir (Paxlovid), remdesivir (Veklury), and molnupiravir (Lagevrio) (CDC, 2022a; NIH, 2022). Oral antivirals, such as nirmatrelvir-ritonavir combination and monlupiravir, are given to adults within five days of onset of symptoms. On the other hand, the most widely used intravenous antiviral among hospitalized patients is remdisivir (Wang et al., 2020). However, early treatment of COVID-19 patients in many countries was recommended with hydroxychloroquine and azithromycin (Million et al., 2020).

MAbs help the immune system recognize and respond more effectively to the virus but are also costly. In addition, they may be more or less effective against different variants or strains of the corona and influenza viruses (NIH, 2017; CDC, 2020a). The immunotherapeutics candidate MAbs CR6261 and CR8020 target the stem region of influenza HA glycoprotein were discovered and developed by Crucell and supported by NIAID can be used to treat influenza. CR621 targets the Flu A Group 1 HA stem, which includes flu types H1, H2, H5, and H9, and CR8020 targets the Flu A group 2 HA stem, which includes H3, H7, and H10 flu subtypes. For COVID-19, Bebtelovimab is an investigational monoclonal antibody treatment used in adults and children ages 12 years and older (NIH, 2022). Bebtelovimab is recommended as a single IV injection and should be started as soon as possible and must begin within seven days of symptoms (NIH, 2022). Tocilizumab (Acmetra) and baricitinib are monoclonal antibodies used in ICU patients and have been proven to have better prognoses (Wang et al., 2020). Convalescent plasma taken from patients who recovered from COVID-19 was also used in severe cases during the pandemic.

Vaccination

Influenza vaccines have been used safely and effectively for more than 60 years. World Health Organization (WHO) recommends vaccination for pregnant women, children (aged between 6 months to 5 years), elderly individuals (aged more than 65 years), individuals with chronic medical conditions, and health-care workers. As the influenza viruses frequently evolves, the WHO Global Influenza Surveillance and Response System (GISRS) continuously survey the viruses circulating in humans and updates the composition of influenza vaccines twice a year. Currently, available influenza vaccines are designed to protect against four influenza viruses: A(H1N1) pdm09 (the 2009 pandemic virus), A(H3N2), B/Victoria lineage, and B/Yamagata lineage. CDC recommends the use of any available influenza vaccines such as quadrivalent inactivated influenza vaccine (IIV4), recombinant influenza vaccine (RIV4), or live attenuated influenza vaccine (LAIV4). Recommended vaccines for 2021-2022 are Flu shots, commercially available, such as Afluria, Fluzone, Fluad (IIV4), Flublock (RIV4), and Nasal spray, Flumist (LAIV4) (CDC, 2021).

Studies on SARS-CoV and MERS-CoV epidemics have helped in developing an effective vaccine on an urgent basis during the COVID-19 pandemic. The S protein protein is the target protein in all types of vaccines developed against SARS-CoV-2 (Tian et al., 2020). Emergency authorization of vaccines has been approved to reduce morbidity and mortality of COVID-19. Several types of vaccines, such as mRNA vaccines (Pfizer and Moderna) and vector-based vaccine (Astrazeneca) inactivated (Sinopharm), has been used worldwide and found to reduce hospital admission (NHS, 2022). At first, two doses were recommended, but an additional booster dose was added with the emergence of new variants. The genomic organization of the virus is continuously being monitored to identify vaccine escape mutants. Vaccine escape mutants of SARS-CoV-2 may increase the need to modify commonly available vaccines. The basic difference in disease mechanism, clinical features, diagnosis, treatment, and vaccination is summarized in Table 2.

Conclusion

Both Influenza and coronaviruses have a long history of emergence and reemergence. The genetic structure of the viruses, as well as their replication capabilities, focuses on their ability to evolve continuously. This mini-review emphasizes the history of pandemics, viral genomes and replication that could influence the creation of the next pandemic potential strain. The review also discussed the current diagnosis, treatment, and vaccination possibilities. However, both viruses are under constant evolution and may have the potential to generate new pandemic strains or variants. As a result, these viruses are under continuous surveillance, and this overview may aid in a quick examination of their biological processes and features.

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