J. Environ. Treat. Tech.
ISSN: 2309-1185

Journal web link: http://www.jett.dormaj.com

Antiviral Pneumonia to Treat Influenza Virus

Sargol Mazraedoost[1,2]*, Seyyed Mojtaba Mousavi[3,1], Seyyed Alireza Hashemi[1,2], Ahmad Gholami[4]

[1]Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran. 71348-14336
[2]Department of Medical Nanotechnology, School of Advanced Medical Sciences and Technologies, Shiraz University of Medical Sciences, Shiraz, Iran
[3]Department of Chemical Engineering, National Taiwan University of Science and Technology, Taiwan
[4]Pharmaceutical Sciences Research Center and Department of Pharmaceutical Biotechnology, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran

Received: 03/02/2020 Accepted: 13/03/2020 Published: 20/05/2020

Abstract

Influenza, an infectious disease of the respiratory system, represents a tremendous sized burden for public health. Influenza was once found not through a direct learn about the disorder in humans, but as a substitute from research on animal diseases. An ailment that can resemble the frequent cold, influenza packs a powerful and on occasion deadly punch. As numerous as half-a-million people around the world die yearly from flu. The perpetrator is a virus that mutates to steer clear of our immune systems, leaving vaccines and remedies scrambling to preserve up. In many years, a mutation creates a pathogen that is specifically nasty, ensuing in pandemic flu. Influenza is an acute respiratory disorder brought on by using the influenza A or B virus. It often happens in outbreaks and epidemics worldwide, frequently in the course of the iciness season. Significant numbers of influenza virus particles exist in the respiratory secretions of infected persons so that infection can be transmitted via sneezing and coughing using large-particle droplets. The imply duration of influenza virus shedding in immunocompetent adult patients is around 5 days but may also proceed for up to 10 days or further mostly in children, elderly adults, patients with chronic illnesses, and immunocompromised hosts. Influenza generally starts with the abrupt onset of high-grade fever, myalgia, headache, and malaise. These manifestations are attended by way of signs of respiratory tract ailments such as non-productive cough, sore throat, and nasal discharge. After an ordinary course, influenza can affect different organs such as the lungs, brain, and heart more than it can affect the respiratory tract and motive hospitalization. The excellent way to stop influenza is to administer annual vaccinations. For centuries, new strains of influenza have emerged to produce human pandemics, inflicting massive illness, death, and disruption. There have been four flu pandemics within the earlier hundred a long time. Throughout this time, globalization processes, globalisation processes, alongside advances in medicine and epidemiology, have altered the way these pandemics are experienced.

Keywords: Pandemic; Influenza; Human; Infectious disease

1 Introduction

Influenza is a transmittable viral illness that influences the apex respiratory tract, which envelops the upper and point of respiratory confinement sections. It is accelerated by methods for utilizing an enormous range of Influenza infections. A portion of these infections can infect people, and some are specific to notable species. These infections are transmissible through respiratory beads ousted from the mouth and respiratory machine all through hacking, talking, and sniffling. The influenza disease can be transmitted by the ability to contact lifeless things dirtied with the infection and contacting the nostril or eye. Influenza can be transmitted heretofore than the influenced individual is symptomatic and till 5 to 7 days after disease. After disease, it takes a couple of days for the majority of the empowering unfortunate casualties to show signs of improvement. Ultimately, on the other hand, inconveniences that comprise of pneumonia and death toll are visited in positive high-chance gatherings. These associations incorporate more youthful kids, old, immunocompromised, and pregnant females. Indications of flu comprise of a runny nose, high fever, hack, and sore throat. Flu spreads and effectively in occasional pandemics. Influenza scourges occur every single harvest time and snowy climate in mild zones and influence a massive factor of grown-ups and youngsters, anyway seasons in an alternate way sway age associations and seriousness (Fig 1) (1-4).

2 Etiology

Influenza viruses belong to the household of viruses termed "Orthomyxoviridae," an RNA kind virus with various antigenic characteristics. They are divided into three most important types: A, B, and C (Fig 2). Furthermost of the epidemics and outbreaks of influenza are induced by types A and B, with type C being commonly accountable for sporadic moderate-higher respiratory symptoms (5, 6). Infections have round or filamentous shapes with an envelope, containing glycoproteins and a single-stranded RNA quality. The 2 most extraordinary fundamental glycoproteins over the outer layer of this season's flu virus disease are hemagglutinin (H, or HA) and neuraminidase (N, or NA). The two include quintessential parts inside the pathogenesis of the sickness. For flu kind A, at slightest sixteen in specific variable hemagglutinins (H1 to H16) and 9 unimaginable NAs (N1 to N9) have been analyzed so distant.

Corresponding author: Seyyed Alireza Hashemi**,** (a) Pharmaceutical Sciences Research Center, Shiraz University of Medical Sciences, Shiraz, Iran. 71348-14336. (b) Department of Medical Nanotechnology, School of Advanced Medical Sciences and Technologies, Shiraz University of Medical Sciences, Shiraz, Iran.

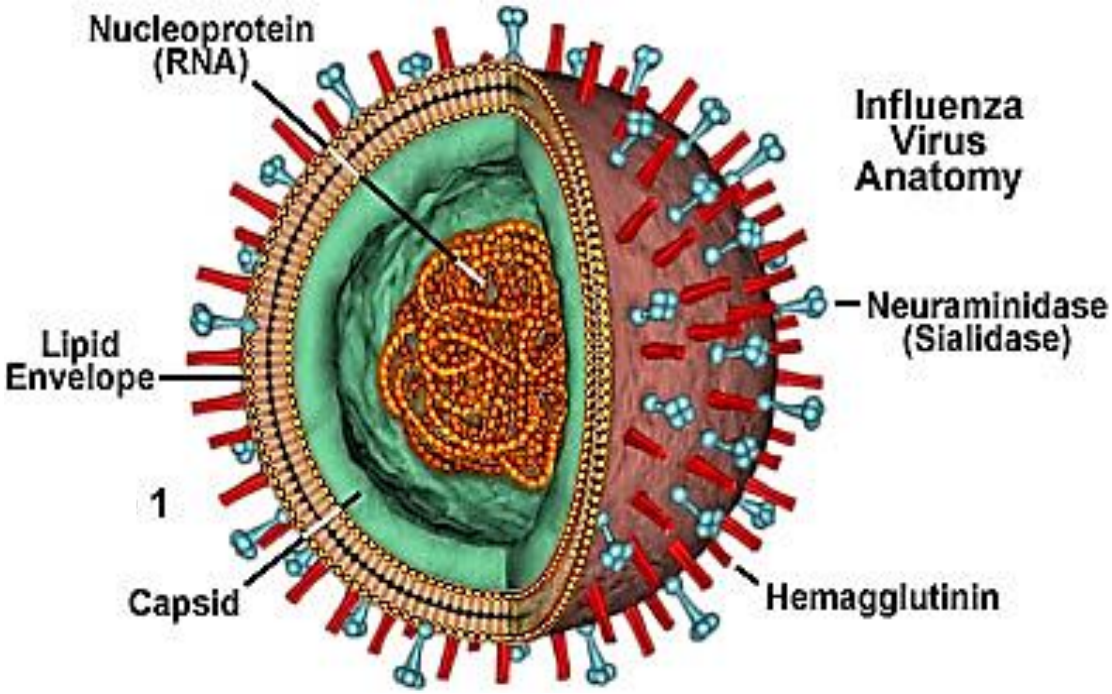

Fig 1. Structure of the influenza virus. 3D illustration displaying floor glycoprotein spikes hemagglutinin blue and neuraminidase green, M2 protein red, capsid made of M1 protein pink and eight fragments of RNA

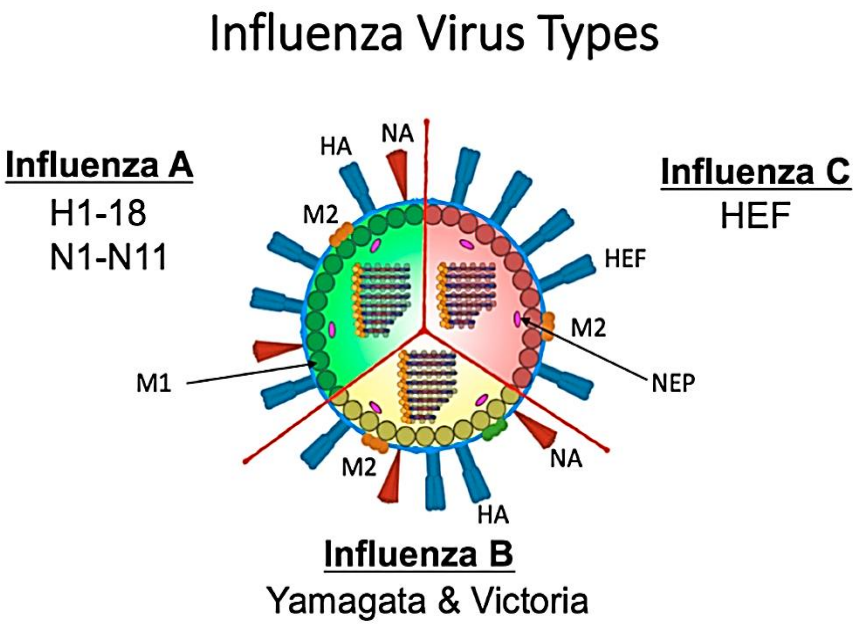

Fig 2. Influenza virus type

With the valuable asset of this one of a shape antigen, the flu sort A infection is mainly subdivided into subtypes based on total variable designs of their impressive H or N proteins (e.g., H1N1 or H3N2). By the by, within the terminology of the infections, other factors for illustration the locale of preparatory confinement and the yr of segregation are covered (7-10). The influenza B virus has a related viral form to form A; however, due to the constant antigenic characters of HA and NA, there are no subtypes in this virus. Still, some small antigenic variabilities have been stated on account that 1970 in this virus, with the virus, had started out to diverge into 2 antigenically awesome lineages (11).

3 Epidemiology

Researchers isolated Influenza A in 1933, seven years later, they remoted influenza B. Influenza viruses in specific geographic areas of the northern and southern hemispheres are recognized as an influenza epidemic which takes place every yr at some stage in the winter seasons.

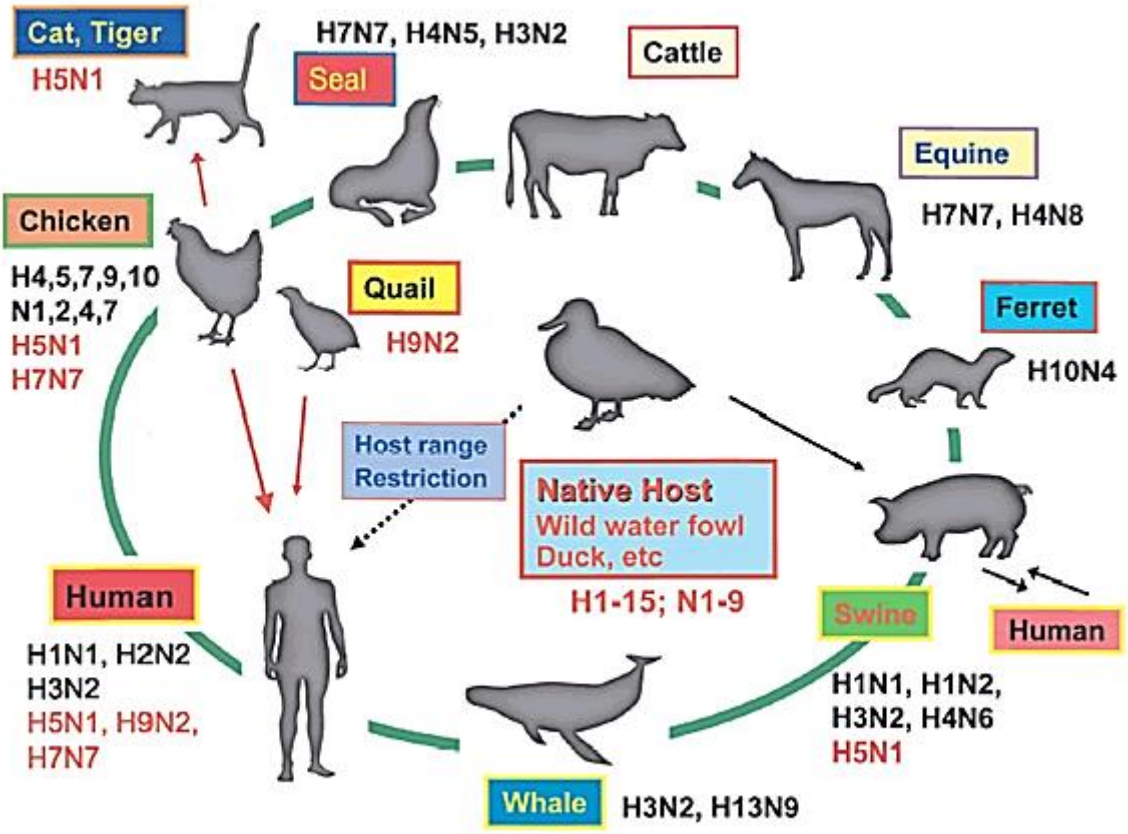

Fig 3. Summary of the ecology of influenza viruses (12)

The severity, size of influenza, and age organizations that are profoundly impacted and complication expenses such as hospitalizations and deaths range substantially all via one of a kind influenza seasons. When H3N2 viruses predominate, the season tends to be extra extreme, particularly amongst youth and the elderly. World Health Organization (WHO) conducts world influenza virologic surveillance that shows influenza viruses are isolated each month from human beings in a geographic region. In temperate regions, influenza endeavour peaks for the duration of the wintry weather months.

4 Transmission

In the respiratory secretion of the sufferers struggling from influenza, massive amounts of virus load are often present, and, as a result, each contaminated man or woman can be transmitting contamination to other folks by sneezing and coughing. It has been posited that the disorder is transmitted notably through large-particle droplets (>5 μ).(13) Owing to the large dimension of infectious droplets, shut contact is wished for the acquisition of the disease. These large particles usually do not continue to be suspended in the air for a lengthy time, and they tour only quick distances. Airborne transmission is, therefore, now not often regarded for disorder unfold (14, 15). Though confined data exhibit that small particle respiratory droplets, which emerge as aerosolized and can stay deferred in the air for a long time, also contain the influenza virus and can potentially cause disease to unfold (16). In the latest study, aerosol transmission accounted for around half of all the transmission events. This suggests that activities to minimize transmission with the aid of contact or large droplets may additionally not be sufficient to manage the transmission of the influenza A virus in households or communities (17). Consequently, the prevention techniques that are drawn automatically in hospitals involve further re-evaluation. Furthermore, contact with contaminated surfaces containing respiratory droplets is some other practicable supply of ailment transmission. In adults barring other underlying diseases, the shedding of the virus begins from 24 to forty-eight hours earlier than disorder manifestation, and the shedding stops after 6 or 7 days according to most research and after 10 days in accordance with some other investigations (18). It is viewed that longer intervals of shedding and infectiousness can occur in children, elderly adults, immunocompromised hosts, and patients with chronic illnesses (Fig 3) (12, 19).

5 Complications of Influenza

5.1 Pneumonia

The most critical and frequent complication of influenza is pneumonia, now not least in high-risk individuals. Pneumonia may also appear as a continuum of the acute influenza syndrome when induced using the influenza virus (primary pneumonia) or as a blended viral and bacterial contamination after a hole of a few days (secondary pneumonia).

5.2 Primary Influenza Viral Pneumonia

The illness happens after the regular route of influenza with the quick development of fever, dyspnea, cough, cyanosis, and challenging breathing. It takes place predominantly amongst individuals with cardiovascular or underlying pulmonary ailments such as asthma. Physical examination is in pick out of bilateral lung involvement, and imaging findings in the lungs represent reticular or reticulonodular opacities with or barring superimposed consolidation. Sometimes the radiological look of primary influenza pneumonia can be challenging to distinguish from pulmonary edema due to the truth of the presence of perihilar congestion and hazy opacification, at least

in the minimize lobes. Less commonly, radiographs demonstration focal zones of infiltration (20-22).

Commonly used pneumonia severity evaluation equipment such as the CURB65 or the Pneumonia Severity Index are not beneficial in finding out which patients to hospitalize due to primary influenza pneumonia, considering that these tools have now not been developed and validated at some point of an influenza pandemic (23). Therefore, the sickness occurs after the ordinary course of influenza with the quick development of fever, dyspnea, cough, cyanosis, and severe breathing. It takes place predominantly amongst humans with cardiovascular or underlying pulmonary illnesses such as asthma. Physical examination is in pick out of bilateral lung involvement, and imaging findings in the lungs signify reticular or reticulonodular opacities with or except superimposed consolidation. Sometimes the radiological seems to be of fundamental influenza pneumonia can be challenging to distinguish from pulmonary edema due to the truth of the presence of perihilar congestion and hazy opacification, at least in the reduce lobes. Less frequently, radiographs demonstrate focal areas of infiltration (24). The most severe instances grow swiftly to acute respiratory misery syndrome and multilobar alveolar infiltrations. These patients are ordinarily current with new dyspnea and extreme hypoxemia 2 to 5 days after the onset of common influenza symptoms. Hypoxemia will increase swiftly and causes respiratory failure, requiring intubation and mechanical ventilation, possibly after solely one day of hospitalization (25, 26).

2.3 Secondary Bacterial Pneumonia

The occurrence of secondary bacterial pneumonia extended from 2% to 18% throughout the influenza pandemic in 1957–58 (27). A threefold amplify in the incidence of secondary Staphylococcus aureus pneumonia during the influenza pandemic of 1968–9 compared to a non-epidemic length of pneumonia etiologies was determined (28).

As of late, community-acquired methicillin-resistant Staphylococcus aureus was decided after regular influenza (29); in any case, another widespread etiologic bacterium is Streptococcus pneumonia. The influenced character encompasses a first influenza disease, went with through potential of an enhancement length enduring maximally 2 weeks. The rehash of the side impacts, for illustration, fever, useful hack, and dyspnea and disclosures of unused unions in chest imaging, can be found in included patients.

2.4 Non-Pulmonary Complications

Regardless of its respiratory impacts, the disease can apply results for unmistakable body structures, for the case, the musculoskeletal, cardiovascular, and neurologic systems. Myocarditis and pericarditis speak to abnormal at that point once more critical issues of regular or widespread influenza. In a planned consider, half of grown-up flu sufferers but cardiac complaints had beat score ECG discoveries at introduction (30). Myocarditis, for the most part, settles by 28 days, and the patients include a great heart-muscle work without a diminished launch division. Noteworthy myositis and rhabdomyolysis have seldom been detailed with regular flu (31), but diverse sums of creatine phosphokinase rise have been detailed in numerous considers after conventional or widespread flues (32, 33). Mellow myositis and myoglobinuria with delicate leg or back muscles can primarily be seen in children, the when all is said in done specificities achieved by these tests are tall and practically identical between the makers. In any case, their sensitivities have seemed magnificent heterogeneity over considers relying upon the idea of the tests attempted and the patients, reaching out from 4.4% to 80% in contrast with cell culture as the best quality level test.

3 Diagnosis

Their clinical appearances analyze the lion's share of influenza cases, and there is no requirement for research facility tests. Be that because it may, in uncommon circumstances, the conclusion of influenza requires research facility affirmation utilizing available tests such as corrosive nucleic tests (e.g., polymerase chain response [PCR]) or quick determination units or once in a while infection segregation by culture strategies.

3.1 Rapid Diagnosis Influenza Tests

Quick influenza symptomatic tests distinguish flu viral antigens and screen patients with suspected influenza conveniently in comparison to other demonstrative modalities. The first broadly utilized method is based on the detection of viral antigens within the respiratory emissions of patients by immunologic strategies. All quick tests are performed with ease and can give comes about inside 30 minutes. Each test changes concerning whether it can recognize between influenza A and B. In any case, these tests have hence distant been incapable of indicating sorts of flu A, such as H1N1 and H3N2. Then when all is said in done, specificities achieved by these tests are tall and practically identical between the makers. In any case, their sensitivities have seemed magnificent heterogeneity over considers relying upon the idea of the tests attempted and the patients, reaching out from 4.4% to 80% in contrast with cell culture as the best quality level test (33-35). As a familiar concept, affectability in grown-ups is less than that detailed in more youthful patients.

Furthermore, the affectability may be higher at the onset of the malady, when the next stack of the infection exists. Financial thinks about comparing fast testing to the clinical determination of influenza stay uncertain. Without a doubt, a few considers have proposed that, in most cases, clinical judgment combined with antiviral treatment is the foremost cost-effective procedure (36), whereas unused ponders have proposed that testing may be the foremost cost-effective methodology and appeared that oseltamivir treatment based on the point-of-care (POC) test could be a prevailing alternative compared to customary approaches without screening tests within the pattern situation which they can be cost-effective in 80% of cases concurring to the cost-effectiveness worthiness bend. Besides, influenza antiviral treatment based on POC may well be cost-effective in particular conditions of execution, cost, and infection predominance (37).

3.2 Molecular Tests

Due to the restriction in other demonstrative modalities in influenza location, atomic tests have progressively been considered the gold standard symptomatic strategy for the location of the influenza disease in healing center based demonstrative research facilities. Even though a few enhancement strategies have been created, the more significant part of the current assays—particularly those utilized in clinical laboratories—is based on the PCR enhancement strategy. These tests can check a few targets concurrently and subsequently give sort and subtype data for each infection. Furthermore, they can be adjusted quickly for the location of novel targets; these highlights (38) played a primary part amid the influenza widespread of 2009. PCR is possibly more delicate than cell culture, and it can distinguish the nonviable infection in tests. The affectability of these tests is subordinate to the test location of the understanding and is comparable to that of the fast tests. Swab tests of a nasopharyngeal beginning can get higher affectability.

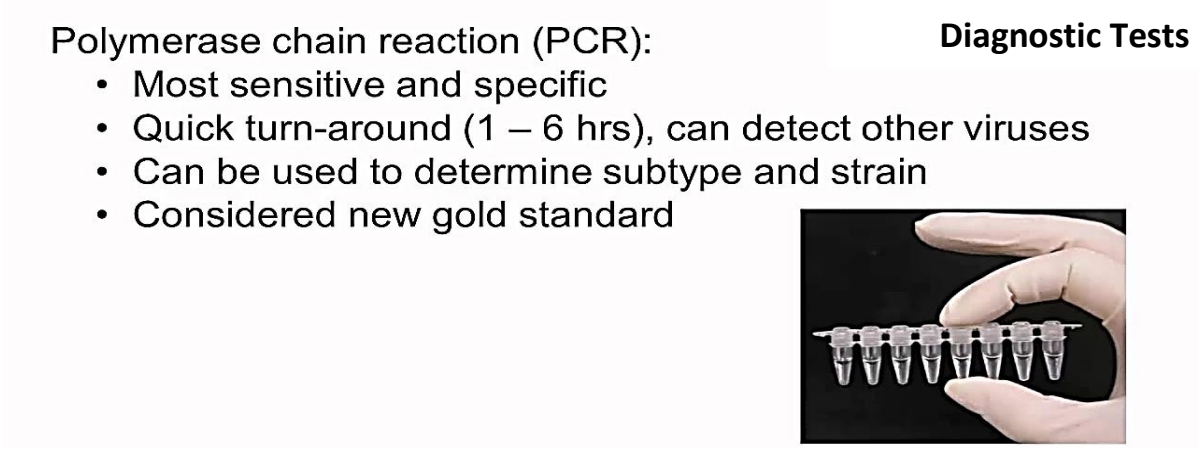

Fig 4. Diagnostic Tests

PCR-based atomic measures have yielded fabulous clinical utility for the discovery and distinguishing proof of influenza disease at the bedside as POC, and various Nourishment and Sedate Organization (FDA)-cleared commercial gadgets are presently accessible (39-41).

4 Part of the Research facility Conclusion of Flu in Clinical Case Administration

Given the self-limiting nature of the infection in something else reliable people, there is no requirement for demonstrative tests in all showing cases. Demonstrative tests ought to be conducted in case the comes about of the test is thought to be able to impact consequent clinical administration, and in case the comes about of the test are regarded persuasive in choices on the start of particular antiviral treatment, effect on other symptomatic tests, anti-microbial treatment decision-making, and contamination control practices (42, 43). Moreover, amid influenza seasons, hospitalized people of any age with fever and extreme respiratory symptoms—including those with a conclusion of community-acquired pneumonia—need research facility testing independent of time from ailment onset.

5 Rapid Influenza Antigen (Nasal or Throat Swab)

What is this test? This test rapidly checks for signs of the influenza viruses A and B in a sample of secretions from your nose or throat. Influenza or the "flu" is an illness of the respiratory system. Influenza A is further common than influenza B. It spreads effectively through water beads within the discuss from hacks or sniffles of individuals who are tainted. It regularly influences numerous individuals at the same time throughout fall and winter.

Symptoms of the flu often show up suddenly. This is often about 1 to 4 days after you're tainted. Most individuals will get way better inside some days to less than 2 weeks. But those with a debilitated resistant framework may get serious pneumonia or other genuine issues. Your healthcare supplier can test for the flu in a few ways. This test as a rule gives comes about rapidly. Immunofluorescence is another test and employments a recoloring procedure. Comes about from these tests are not as precise as viral societies. But these tests are speedier and less demanding. They are commonly utilized for the primary screening. You do not continuously require a flu test for your supplier to analyze the flu. Healthcare suppliers may make the determination and start treatment based on your side effects and a physical exam.

6 Pathophysiology

Influenza is an acute infection that points to the upper respiratory tract and thought processes disease of the upper respiratory tree and trachea. The great signs endure for seven to ten days, and the sickness is self-limited in most solid people. The resistant reaction to the viral disease and the intergalactic reaction is dependable for the viral disorder that incorporates over the top fever, coryza, and physical make-up hurts. High-risk companies who have nonstop lung illnesses, cardiac illness, and being pregnant are higher slanted to extraordinary inconveniences such as imperative viral pneumonia, auxiliary bacterial pneumonia, hemorrhagic bronchitis, and passing. These extraordinary inconveniences can upgrade in as small as forty-eight hours from the beginning of indications. The infection duplicates within the more prominent and diminishes respiratory sections starting from the time of immunization and cresting after forty-eight hours, on average.

7 Viral entry: How does the virion enter the host?

The excellent way in which influenza is transmitted is from individual to individual by mist concentrates and beads. Influenza at that point enters the have through the respiratory tract. In a human lung, there are almost 300 million terminal sacs, called alveoli, that work in vaporous trade between motivated discussion and the blood—the entire absorptive region of the human lung ranges from 80-120 m2. The resting ventilation rate in people is around 6 liters of discussing per miniature, which presents enormous numbers of outside particles and aerosolized beads, possibly containing infection into the lungs. Testimony of outside particles depends on their estimate: inward breath of tiny particles does not result in assimilation through the alveoli or bronchial framework. Little beads with a breadth of approximately 1 to 4 μm accelerate within the little aviation routes. Much bigger particles are either not able to enter the respiratory contraption or are kept within the best respiratory tract (Figure 5A).Various have defense components comprising of mechanical deterrents piece respiratory tract disease. The respiratory tract is included with a mucociliary layer comprising of ciliated cells, mucus-secreting cells, and organs (Figure 5B). Outside particles within the nasal depth or best respiratory tract are caught in the bodily fluid, carried lower back to the throat, and gulped. From the diminish respiratory tract, foreign particles are brought up by way of the ciliary action of epithelial cells. Within the alveoli that need cilia or bodily fluid, macrophages are dependable for wrecking particles (Figure 5).

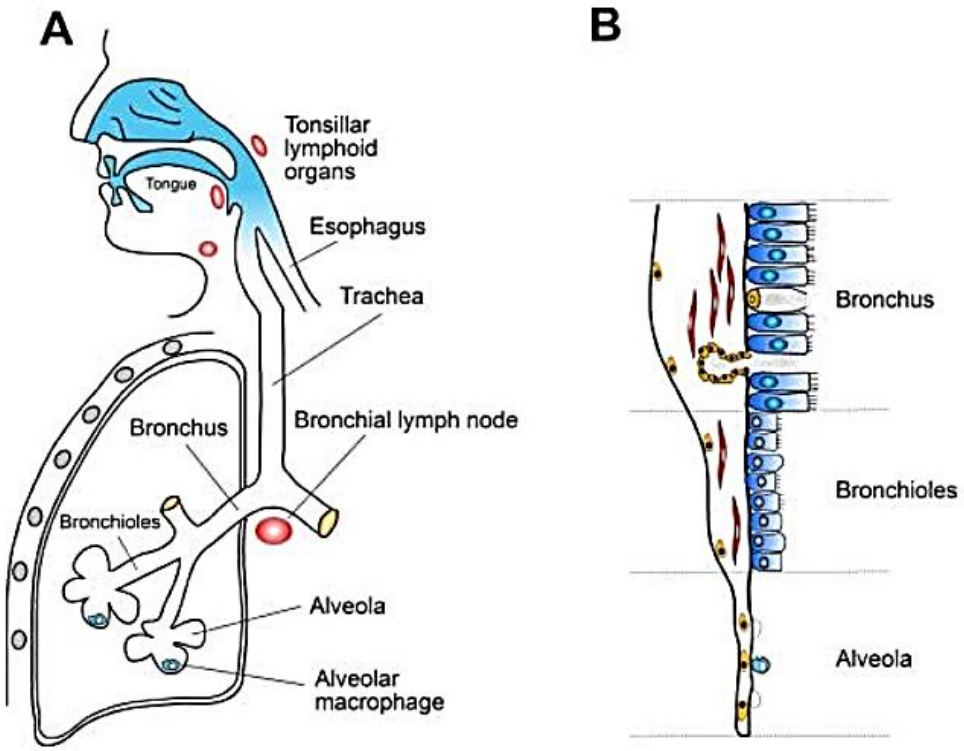

Fig 5. Locales of the influenza section within the respiratory tract. (A) The anatomical and viable structures of the human aviation routes appear. Influenza, to begin with, contaminates the higher aviation route and the ciliated cells within the bronchus and bronchioli. Coming about logical disorders comprise of tracheitis, bronchitis, bronchiolitis, and bronchopneumonia. The versatile, safe reaction is started in lymph hubs nearby the aviation routes. (B) The respiratory epithelia are primarily outfitted to watch from approaching pathogens using a layer of bodily fluid (bronchus), ciliated cells (bronchus and bronchioli), and alveolar macrophages (alveoli) (42).

8 Histopathology

Influenza disease imitate within the epithelial phone lining of the beat and lower respiratory tracts. The pathology does no longer extend between home grew or test contamination. Conclusive conclusion of influenza serologic, immunologic, and atomic testing through RT-PCR for higher or lower respiratory tract examples. Mellow cases grandstand neurotic changes within the respiratory tracts; in any case, extreme occurrences exhibit explicit confirmation of pathologic alterations of pneumonia. The tracheobronchial changes due to influenza contamination can be summarized as redness and contamination with mucous and purulent discharge macroscopically, and desquamation and destruction of the pseudostratified epithelium of the trachea and bronchi with ultimately the basal layer remained viable however infected microscopically (44).

9 Immunology

Influenza causes intense contamination of the have and starts a cascade of safe responses enacting about all parts of the resistant defense framework. Most of the initial natural reaction, comprehensive of cytokine discharge (IFNα/β), influx of neutrophil granulocytes, or healthy executioner cells (45-47), and cell actuation, is dependable for the intense onset of the clinical indications (see over). Natural resistance is a fundamental prerequisite for the versatile resistant reaction, firstly, to constrain the starting viral replication and antigen stack, and since the antigen-specific lymphocytes of the versatile resistant reaction are enacted by co-stimulatory atoms that are initiated on cells of the intrinsic resistant framework amid their interaction with infections (Figure 6). Influenza diseases, in any case, encode inside the non-basic protein 1 (NS1) segments to keep away from and offend the IFN α/β response. NS1 is likely to sequester viral dsRNA, which avoids acknowledgment of this perilous atom by cellular sensors, which would something else trigger IFN α/β discharge (48-51).

The flexible, safe response requires several days to be better than average, but at that point makes a distinction to contain the viral spread, to destroy the disease, and at final to set up a memory response coming approximately in a long-lived resistance to re-infection with the homologous disease. Cross-protection interior, a subtype of flu, has only scarcely ever been found, and contaminations truly set off no confirmation over subtypes or between sorts A and B (Treanor 2005). Flu contamination activates each systemic and neighbourhood counteracting specialist (humoral insusceptibility), as fittingly as cytotoxic T convenient responses (cellular insusceptibility), each of which is fundamental in patching from strongly debasement and resistance to reinfection (52, 53).

10 Therapy

Right now, at slightest four antiviral capsules are helpful for the treatment and avoidance of flu. It is meriting of being mindful that in energizing immunocompetent people with intaglio resistance, there is a fast inconvenience within the capability of the flu infection; hence, the subterranean insect replication control of antiviral tablets is constrained and has no hypothetical impact. Too, no think about to date has confirmed a useful effect for antiviral retailers starting the past 48 hours of indication onset. The most prominent effect is classically viewed when cure is begun out within the, to begin with, 24 hours. Treatment is embraced for each grown-up and kids with the flu infection defilement with the taking after criteria: 1) persons with laboratory-confirmed or distinctly suspected influenza virus contamination in high-risk corporations (table 1), inside 48 hours after symptom onset; 2) patients requiring hospitalization for laboratory-confirmed or outstandingly

suspected flu infection, in any case of fundamental ailments, in case treatment can be started inside 48 hours after side effect onset; and 3) outpatients at high chance of issues (table 1) with a sickness that's not making strides and outpatients with high-quality flu take a see at conclusion result from an example gotten >48 hours after side effect onset. Individuals whose onset of signs is >48 hours sometime recently introduction with continuing moderate-to-severe illness.

Amid the final widespread wave, neuraminidase inhibitors (NAIs)—primarily oseltamivir and zanamivir—were broadly endorsed for patients with affirmed or suspected A H1N1pdm09 infection (54-56). Be that as it may, sometimes newly the 2009–10 widespread, prove of their adequacy in regular flu, whereas reliable for unassuming indication diminishment, was less reliable for diminishes in pneumonia rate or pneumonia result change (57-60). Later information illustrated that patients with influenza-related pneumonia treated early after ailment onset) with an NAI experienced around one-third lower probability of biting the dust or requiring ventilator help compared to those treated at afterward hours (15, 61). Influenza viruses and their susceptibilities to available antiviral drugs are changing quickly. Clinicians ought to be mindful of the nearby designs of flu circulations and susceptibilities. For occurrence, a meta-analysis appeared that NAIs were able to reduce mortality in patients conceded to the healing center with An H1N1pdm09 disease. Scattered oseltamivir-resistant contaminations have been recognized, along with different side scenes of restricted transmission (62). Given the as of now circulating flu A (H3N2) and 2009 H1N1 infection resistance to adamantanes, these solutions are not suggested for utilizing against flu A virus-induced diseases. Be that as it may, most influenza A and B infection strains are still vulnerable to neuraminidases, for example, oseltamivir and zanamivir, with these drugs being chosen for treatment in demonstrated people (table 2). In expansion, it ought to be considered that the improvement of resistance to oseltamivir amid treatment was more common among regular flu A (H1N1) infection contaminations (27%) than among regular influenza A (H3N2) (3%) or B (0%) infection contaminations in a later ponder (63). Due to the confinements within the current restorative alternatives for the treatment of influenza.

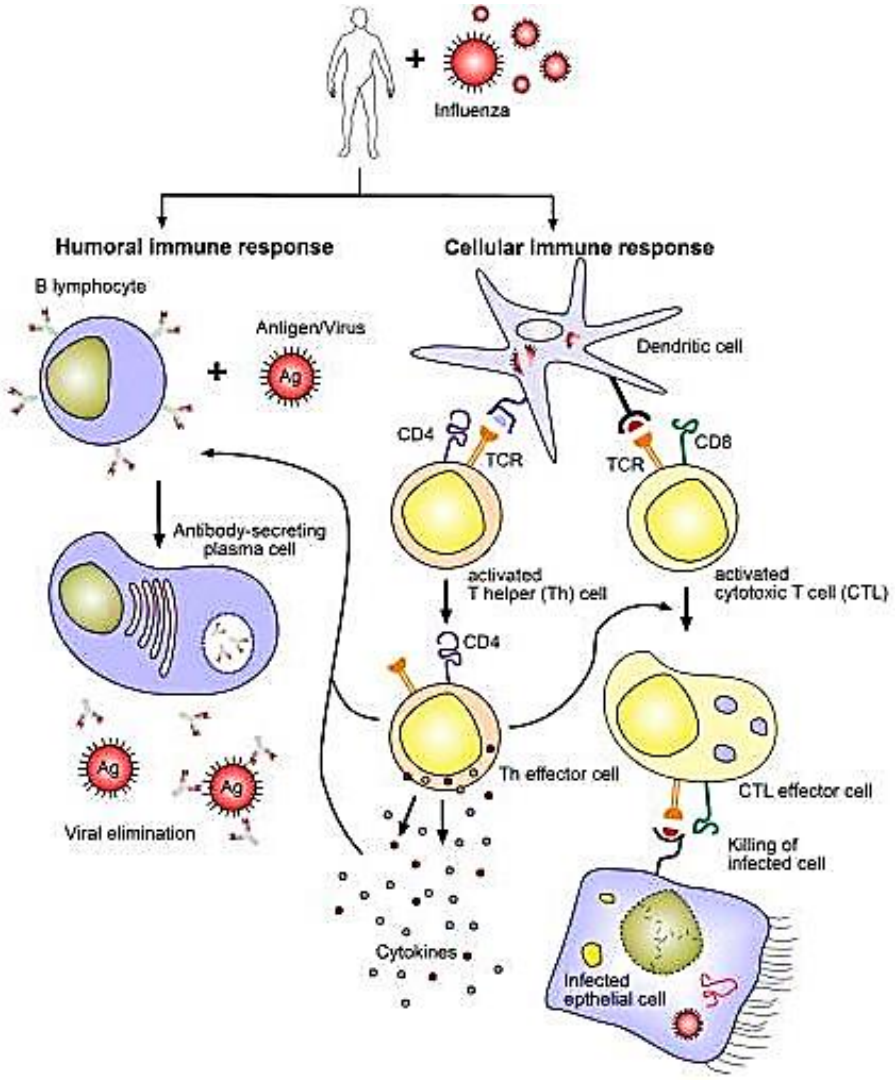

Fig 6. Innate immunity is a necessary prerequisite for the versatile resistant reaction, firstly, to constrain the starting viral replication and antigen stack, and since the antigen-specific lymphocytes of the versatile resistant reaction are enacted by co-stimulatory atoms that are actuated on cells of the safe, natural framework amid their interaction with viruses.

Table 1: Recommended dosages and durations of influenza antiviral medications for treatment or chemoprophylaxis

Antiviral agent	Use	Adults
Oseltamivir	Treatment (5 d)	75 mg twice daily
	Chemoprophylaxis (7 d)	75 mg once daily
Zanamivir	Treatment (5 d)	10 mg (two 5-mg inhalations) twice daily
	Chemoprophylaxis (7 d)	10 mg (two 5-mg inhalations) once daily

Virus infections, extra treatment choices with a diverse instrument of activity have been examined as a treatment for people with extreme influenza infection. For the case, a modest bunch of mAbs against influenza infection proteins are as of now within the early stages of assessment for human disease control (64). These mAbs target the external portions (i.e., ectodomain) of the M2 protein (M2e). These mAbs target the outside parcels (i.e., ectodomain) of the M2 protein (M2e). The M2e is an alluring target for influenza immunizations and therapeutic antibodies since the significantly moderated nature of the corrosive amino groupings of its spaces among separates from diverse subtypes of influenza A viruses (65).

The instruments of anti-M2e Ab–mediated assurance is not determined. Anti-M2 Abs do not have hemagglutination restraint capacity or in vitro infection neutralization properties (66). It is assumed that the most target for the hostile to- M2e counter acting agent is virus-infected human cells, which intensely express M2e on their surface (67). Most considers have detailed that corticosteroid treatment unfavorably impacts influenza-related results. Amid the 2009 flu widespread, 37% to 55% of the patients conceded to ICUs in Europe gotten corticosteroids as a portion of their treatment (68-70). In any case, in a later meta-analysis report, prove from observational studies—albeit with essential limitations— recommended that corticosteroid treatment for assumed influenza-associated complications was related to expanded mortality (71).

11 Clinical trials with influenza antiviral drugs

Most individuals with flu have gentle ailment and don't require restorative care or antiviral drugs. On the off chance that you basically get weakened with flu side effects, in most cases, you have to be stay residential and keep up a key separate from contact with other individuals but to actuate restorative care. If, in any case, you have got side effects of flu and are in a high-risk bunch, or are exceptionally debilitated or stressed approximately your sickness, contact your wellbeing care supplier (specialist, doctor collaborator, etc.). CDC suggests provoke treatment for individuals who have flu contamination or suspected flu contamination and who are at tall hazard of genuine flu complications, such as individuals with asthma, diabetes or heart disease (72).

12 You might need antiviral medication to treat flu:

- Antiviral drugs can treat flu illness
- Antiviral drugs are different from antibiotics. Flu antivirals are prescription medicines (pills, liquid, intravenous solution, or an inhaled powder) and are not available over-the-counter
- Antiviral drugs can make ailment milder and abbreviate the time you're wiped out. They too can anticipate genuine flu complications, like pneumonia
- It's very significant that antiviral drugs be used early to treat people who are very sick with flu (for instance, people who are in the hospital) and people who are wiped out with flu and have a more noteworthy chance of getting genuine flu complications, either since of their age or since they have a tall hazard therapeutic condition. Other individuals too may be treated with antiviral drugs by their specialist this season. Most otherwise-healthy individuals who get flu, be that as it may, don't have to be be treated with antiviral drugs.

13 Prevention

13.1 Vaccination

The first vital methodology for the anticipation of influenza and its serious results is yearly immunization against regular flu. The influenza infection is characterized by its high rate of transformation, beating the safe system's work against unused variations (73), which is why novel vaccines are produced annually to match circulating viruses (74). The choice of influenza antigens to incorporate within the antibodies is based upon the worldwide reconnaissance of flu infections in circulation and the spread of available strains of the influenza disease around the world (75). For the subsequent influenza season within the southern side of the equator, proposals are made in September and for the influenza season within the northern side of the equator in February since around 6 to 8 months are required to fabricate and approve novel immunizations. Recently, the World Wellbeing Organization (WHO) suggested that trivalent influenza immunizations for utilize within the 2016 southern half of the globe flu season contain the taking after infection antigens(76):

- An A/California/7/2009 (H1N1) pdm09-like virus
- An A/Hong Kong/4801/2014 (H3N2)-like virus
- A B/Brisbane/60/2008-like virus
- The WHO stresses that vaccination is particularly vital for people at higher hazard of genuine flu complications, with the most noteworthy need managed to pregnant ladies—taken after by children matured between 6 and 59 months, elderly and people with particular unremitting restorative conditions (e.g., renal disappointment and diabetes mellitus), and at last people at tall chance (e.g., wellbeing staff) (77).

In differentiate in 2010, the Joined together States' Counseling Committee on Immunization Hones (ACIP) expanded the proposal for yearly influenza immunization to include all people six months of age and more seasoned people who did not have contraindications without any need (78).

13.2 Schedule

The episodes of flu, by and large, happen amid the final harvest time and entirety winter months. A single dosage (0.5 ccs) of an influenza antibody ought to be infused to grown-ups every year, ideally by October within the northern hemisphere and May within the southern half of the globe. Children matured between 6 months and eight a long time require two dosages of flu antibody (with at slightest four weeks separated) amid their first season of immunization for the typical reaction (78).

13.3 Efficacy

The immunization adequacy of flu immunizations may be a determinant of how much the regular influenza vaccine can anticipate flu infection contaminations within the given populace amid an influenza season (79). As of late, the

documentation of the antigenic drift from the antibody weight in the lion's share of respected separates raised the subject that immunization viability may be problematic, primarily in more seasoned a long time or specific high-risk bunches. The Centers for Infection Control and Anticipation (CDC) within the Joined together the States of America had an estimation of 23% of immunization viability for the northern side of the equator 2014–15 regular flu antibody due to a jumble within the circulating infections and antibody contained infections (80).

What ought to be taken into thought is that indeed if an antibody is not wholly related to the overwhelming circulating infection, it can watch various particular flu infections and can, as such, bestow exact assurance and stop influenza-related sicknesses. It is additionally a reality that flu immunizations are secured and are particularly imperative for diminishing severe illness in a few high-risk populaces. In like manner, the WHO suggests regular flu antibodies indeed on the off chance that they are not carefully related to the overwhelming circulating flu infections each year for the organizations mentioned above (24).

14 Chemoprophylaxis Strategy

Accessible antiviral drugs play a vital part in patients who have not been immunized or who are nonresponsive to antibodies. Oseltamivir and zanamivir are the prescribed drugs for the avoidance of influenza based on their built up adequacy and moo rates of resistance in comparison to adamantanes (81, 82). These operators are successful for the anticipation of influenza in reliable people, people at high hazard of flu complications, and those dwelling in long-term care offices. The adequacy of oseltamivir and zanamivir has, however, to be compared with each other (83). It ought to be emphasized that when choosing a technique of antiviral chemoprophylaxis, a few parameters such as anticipating complications in patients at high hazard and lessening the chance of advancing sedate antiviral resistance ought to be considered. There are, hence, a few signs for this approach, as follows (84): 1) Influenza prophylaxis amid influenza episodes in long-term care centers within the elderly notwithstanding earlier influenza vaccinations. 2) In unvaccinated people at the high chance of influenza complications which have been uncovered to a person with influenza diseases inside the past 48 hours. 3) Antiviral prophylaxis for immunized people at the high chance of influenza complications who have had near contact with a person with influenza inside the previous 48 hours when there is a destitute coordinate between the immunization and circulating infections in a given year. 4) The Joined together States' ACIP suggests that antiviral chemoprophylaxis be considered in pregnant women and in women up to 2 weeks postpartum who have close contact with suspected or confirmed influenza A-infected individuals. Zanamivir may be the drug of choice for prophylaxis due to its limited systemic absorption (84, 85).

Medicate resistance got to be respected on the off chance that we select to bargain with all sufferers who are labeled as battling from influenza. People with suspected pipe with an extraordinary affliction such as those with side effects and signs of diminishing respiratory tract contaminations (e.g., dyspnea, tachypnea, and moo oxygen immersion) and these who have side effects of quick clinical deterioration or these at great danger of issues got to get hold of antiviral treatment. In all cases, antivirals ought to be started <48 hours after side effect onset. In pregnant patients due to more noteworthy mortality, there is a counsel that all sufferers with suspected or affirmed influenza-even those who were existing >48 hours after side effect onset—be managed with provided that they are not making strides. In expansion, an unused appear at antiviral chemoprophylaxis, and it's fitting utilize might too influence a markdown in dreariness, and mortality partnered to influenza in high-risk bunches (85).

15 Conclusion

We have considered how flu disease contamination leads to the noteworthy progression of a febrile respiratory affliction. The pathogenesis is characterized by way of the convenient replication and scattering of the disease insides the lungs, causing neighborhood and systemic defilement and cytokine release. These events, collectively with the flexible safe response, offer help to decrease the viral burden, to encourage liberated of the disease, and to set off clutter recovery. The humoral and cellular resistant reactions, incited by way of disease or inoculation, outfit people and populaces with long-lasting cautious insusceptibility in resistance to related viral strains. Influenza, be that as it may, can weaken this contamination- or vaccine-derived insusceptibility through implies of antigenic move and float, coming about in plague and widespread flare-ups. Specialized advancements, alongside hereditary and down to earth ponders, will help to realize a further profound discernment into the pathogenesis of antiquated and directly circulating virulent influenza strains. This understanding and a far reaching acknowledgment roughly the viral safe security disobedient inside the human lung will ideally energize the headway of prevalent treatment choices and more unmistakable high-quality immunizations to be allocated around the world against current and future flu disease varieties.

References

1. Alguacil-Ramos A, Portero-Alonso A, Pastor-Villalba E, Muelas-Tirado J, Díez-Domingo J, Sanchis-Ferrer A, et al. Rapid assessment of enhanced safety surveillance for influenza vaccine. Public health. 2019;168:137-41.
2. Tennant RK, Holzer B, Love J, Tchilian E, White HN. Higher levels of B-cell mutation in the early germinal centres of an inefficient secondary antibody response to a variant influenza haemagglutinin. Immunology. 2019;157(1):86-91.
3. Marshall C, Williams K, Matchett E, Hobbs L. Sustained improvement in staff influenza vaccination rates over six years without a mandatory policy. Infection Control & Hospital Epidemiology. 2019;40(3):389-90.
4. Mousavi S, Zarei M, Hashemi S. Polydopamine for Biomedical Application and Drug Delivery System. Med Chem(Los Angeles). 2018;8:218-29.
5. Mosnier A, Caini S, Daviaud I, Nauleau E, Bui TT, Debost E, et al. Clinical characteristics are similar across type A and B influenza virus infections. PLoS One. 2015;10(9):e0136186.
6. Poon LL, Song T, Rosenfeld R, Lin X, Rogers MB, Zhou B, et al. Quantifying influenza virus diversity and transmission in humans. Nature genetics. 2016;48(2):195.
7. Fuller TL, Gilbert M, Martin V, Cappelle J, Hosseini P, Njabo KY, et al. Predicting hotspots for influenza virus reassortment. Emerging infectious diseases. 2013;19(4):581.
8. Mousavi SM, Hashemi SA, Ghasemi Y, Amani AM, Babapoor A, Arjmand O. Applications of graphene oxide in case of nanomedicines and nanocarriers for biomolecules: review study. Drug metabolism reviews. 2019;51(1):12-41.
9. Mousavi SM, Hashemi SA, Ghasemi Y, Atapour A, Amani AM, Savar Dashtaki A, et al. Green synthesis of silver nanoparticles toward bio and medical applications: review study. Artificial cells, nanomedicine, and biotechnology. 2018;46(sup3):S855-S72.
10. Mousavi S, Hashemi S, Zarei M, Amani A, Babapoor A. Nanosensors for Chemical and Biological and Medical Applications. Med Chem (Los Angeles). 2018;8(8):2161-0444.1000515.
11. Kanegae Y, Sugita S, Endo A, Ishida M, Senya S, Osako K, et al. Evolutionary pattern of the hemagglutinin gene of influenza B viruses isolated in Japan: cocirculating lineages in the same epidemic season. Journal of virology. 1990;64(6):2860-5.

12. Boivin G, Goyette N, Bernatchez H. Prolonged excretion of amantadine-resistant influenza a virus quasi species after cessation of antiviral therapy in an immunocompromised patient. Clinical Infectious Diseases. 2002;34(5):e23-e5.
13. Степанова ЛА, Ковалева А, Потапчук М, Коротков А, Куприянов В, Блохина Е, et al. Иммуногенные свойства рекомбинантных белков, включающих эктодомен белка М2 вируса гриппа а. Вопросы вирусологии. 2013;58(3).
14. Brankston G, Gitterman L, Hirji Z, Lemieux C, Gardam M. Transmission of influenza A in human beings. The Lancet infectious diseases. 2007;7(4):257-65.
15. Mousavi SM, Hashemi SA, Zarei M, Bahrani S, Savardashtaki A, Esmaeili H, et al. Data on cytotoxic and antibacterial activity of synthesized Fe3O4 nanoparticles using Malva sylvestris. Data in brief. 2020;28:104929.
16. Choi W-S, Lee J, Lee H-Y, Baek J-H, Kim Y-K, Kee S-Y, et al. Clinical Practice Guideline for Antiviral Treatment and Chemoprophylaxis of Seasonal Influenza. Infection & Chemotherapy. 2012;44(4).
17. Cowling BJ, Ip DK, Fang VJ, Suntarattiwong P, Olsen SJ, Levy J, et al. Aerosol transmission is an important mode of influenza A virus spread. Nature communications. 2013;4:1935.
18. Wong BC, Lee N, Li Y, Chan PK, Qiu H, Luo Z, et al. Possible role of aerosol transmission in a hospital outbreak of influenza. Clinical infectious diseases. 2010;51(10):1176-83.
19. Carrat F, Vergu E, Ferguson NM, Lemaitre M, Cauchemez S, Leach S, et al. Time lines of infection and disease in human influenza: a review of volunteer challenge studies. American journal of epidemiology. 2008;167(7):775-85.
20. Weinstock DM, Gubareva LV, Zuccotti G. Prolonged shedding of multidrug-resistant influenza A virus in an immunocompromised patient. New England Journal of Medicine. 2003;348(9):867-8.
21. Liu W, Peng L, Liu H, Hua S. Pulmonary function and clinical manifestations of patients infected with mild influenza A virus subtype H1N1: a one-year follow-up. PloS one. 2015;10(7).
22. Rello J, Pop-Vicas A. Clinical review: primary influenza viral pneumonia. Critical Care. 2009;13(6):235.
23. Minodier L, Charrel RN, Ceccaldi P-E, Van Der Werf S, Blanchon T, Hanslik T, et al. Prevalence of gastrointestinal symptoms in patients with influenza, clinical significance, and pathophysiology of human influenza viruses in faecal samples: what do we know? Virology journal. 2015;12(1):215.
24. Vickers NJ. Animal Communication: When I'm Calling You, Will You Answer Too? Current Biology. 2017;27(14):R713-R5.
25. Mancinelli L, Onori M, Concato C, Sorge R, Chiavelli S, Coltella L, et al. Clinical features of children hospitalized with influenza A and B infections during the 2012–2013 influenza season in Italy. BMC infectious diseases. 2015;16(1):6.
26. Bahrani S, Hashemi SA, Mousavi SM, Azhdari R. Zinc-based metal–organic frameworks as nontoxic and biodegradable platforms for biomedical applications: review study. Drug metabolism reviews. 2019;51(3):356-77.
27. Rello J, Rodríguez A, Ibañez P, Socias L, Cebrian J, Marques A, et al. the H1N1 SEMICYUC working group: Intensive care patients with severe novel H1N1 influenza viral pneumonia in Spain. Crit Care. 2009;13:R148.
28. To K, Hung I, Li I, Lee K, Koo C, Yan W, et al. Pandemic H1N1 Study Group: Delayed clearance of viral load and marked cytokine activation in severe cases of pandemic H1N1 2009 influenza virus infection. Clin Infect Dis. 2010;50:850-9.
29. Schwarzmann SW, Adler JL, Sullivan RJ, Marine WM. Bacterial pneumonia during the Hong Kong influenza epidemic of 1968-1969: experience in a city-county hospital. Archives of internal medicine. 1971;127(6):1037-41.
30. Kallen AJ, Brunkard J, Moore Z, Budge P, Arnold KE, Fosheim G, et al. Staphylococcus aureus community-acquired pneumonia during the 2006 to 2007 influenza season. Annals of emergency medicine. 2009;53(3):358-65.
31. Ison MG, Campbell V, Rembold C, Dent J, Hayden FG. Cardiac findings during uncomplicated acute influenza in ambulatory adults. Clinical infectious diseases. 2005;40(3):415-22.
32. Foulkes W, Rees J, Sewry C. Influenza A and rhabdomyolysis. Journal of Infection. 1990;21(3):303-4.
33. Chen K-F, Gaydos C, Rothman RE. Update on emerging infections: news from the Centers for Disease Control and Prevention. Hospitalized patients with novel influenza A (H1N1) virus infection--California. 2009:732-6.
34. Chu H, Lofgren ET, Halloran ME, Kuan PF, Hudgens M, Cole SR. Performance of rapid influenza H1N1 diagnostic tests: a meta-analysis. Influenza and other respiratory viruses. 2012;6(2):80-6.
35. Chartrand C, Leeflang MM, Minion J, Brewer T, Pai M. Accuracy of rapid influenza diagnostic tests: a meta-analysis. Annals of internal medicine. 2012;156(7):500-11.
36. Karthik L, Kumar G, Keswani T, Bhattacharyya A, Chandar SS, Rao KB. Protease inhibitors from marine actinobacteria as a potential source for antimalarial compound. PloS one. 2014;9(3).
37. Nagase H, Moriwaki K, Kamae M, Yanagisawa S, Kamae I. Cost-effectiveness analysis of oseltamivir for influenza treatment considering the virus emerging resistant to the drug in Japan. Value in Health. 2009;12:S62-S5.
38. Nshimyumukiza L, Douville X, Fournier D, Duplantie J, Daher RK, Charlebois I, et al. Cost-effectiveness analysis of antiviral treatment in the management of seasonal influenza A: point-of-care rapid test versus clinical judgment. Influenza and other respiratory viruses. 2016;10(2):113-21.
39. Klugman K. Clinical Microbiology Reviews. Clin Microbiol Rev. 1990;3(2):171-96.
40. Teo J, Di Pietro P, San Biagio F, Capozzoli M, Deng Y-M, Barr I, et al. VereFlu™: an integrated multiplex RT-PCR and microarray assay for rapid detection and identification of human influenza A and B viruses using lab-on-chip technology. Archives of virology. 2011;156(8):1371.
41. Tang Y-W, Lowery KS, Valsamakis A, Schaefer VC, Chappell JD, White-Abell J, et al. Clinical accuracy of a PLEX-ID flu device for simultaneous detection and identification of influenza viruses A and B. Journal of clinical microbiology. 2013;51(1):40-5.
42. Loeffelholz M, Pong D, Pyles R, Xiong Y, Miller A, Bufton K, et al. Comparison of the FilmArray Respiratory Panel and Prodesse real-time PCR assays for detection of respiratory pathogens. Journal of clinical microbiology. 2011;49(12):4083-8.
43. Gholami A, Shahin S, Mohkam M, Nezafat N, Ghasemi Y. Cloning, characterization and bioinformatics analysis of novel cytosine deaminase from Escherichia coli AGH09. International Journal of Peptide Research and Therapeutics. 2015;21(3):365-74.
44. Moghadami M. A narrative review of influenza: a seasonal and pandemic disease. Iranian journal of medical sciences. 2017;42(1):2.
45. Behrens G, Stoll M, Kamps B, Hoffman C, Preisser W. Pathogenesis and immunology. Monografía en Internet] Flying Publisher Cologne, Holland. 2006;19.
46. Mandelboim O, Lieberman N, Lev M, Paul L, Arnon TI, Bushkin Y, et al. Recognition of haemagglutinins on virus-infected cells by NKp46 activates lysis by human NK cells. Nature. 2001;409(6823):1055-60.
47. Mousavi SM, Zarei M, Hashemi SA, Babapoor A, Amani AM. A conceptual review of rhodanine: current applications of antiviral drugs, anticancer and antimicrobial activities. Artificial cells, nanomedicine, and biotechnology. 2019;47(1):1132-48.
48. García-Sastre A, Egorov A, Matassov D, Brandt S, Levy DE, Durbin JE, et al. Influenza A virus lacking the NS1 gene replicates in interferon-deficient systems. Virology. 1998;252(2):324-30.
49. Tumpey TM, Basler CF, Aguilar PV, Zeng H, Solórzano A, Swayne DE, et al. Characterization of the reconstructed 1918 Spanish influenza pandemic virus. science. 2005;310(5745):77-80.
50. Abbaszadegan A, Dadolahi S, Gholami A, Moein MR, Hamedani S, Ghasemi Y, et al. Antimicrobial and cytotoxic activity of Cinnamomum zeylanicum, Calcium Hydroxide, and triple antibiotic paste as root canal dressing materials. The journal of contemporary dental practice. 2016;17(2):105-13.
51. Gholami A, Rasoul-Amini S, Ebrahiminezhad A, Abootalebi N, Niroumand U, Ebrahimi N, et al. Magnetic properties and antimicrobial effect of amino and lipoamino acid coated iron oxide nanoparticles. Minerva Biotecnologica. 2016;28(4):177-86.
52. Mousavi SM, Soroshnia S, Hashemi SA, Babapoor A, Ghasemi Y, Savardashtaki A, et al. Graphene nano-ribbon based high potential and efficiency for DNA, cancer therapy and drug delivery applications. Drug metabolism reviews. 2019;51(1):91-104.
53. Abbaszadegan A, Gholami A, Abbaszadegan S, Aleyasin ZS, Ghahramani Y, Dorostkar S, et al. The effects of different ionic liquid coatings and the length of alkyl chain on antimicrobial and

cytotoxic properties of silver nanoparticles. Iranian endodontic journal. 2017;12(4):481.
54. Muthuri Stella G, Sudhir V, Myles Puja R, Jo L-B, Al Khuwaitir Tarig S. Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data. Lancet Respir Med. 2014;2(5):395-404.
55. Gasparini R, Amicizia D, Lai PL, Bragazzi NL, Panatto D. Compounds with anti-influenza activity: present and future of strategies for the optimal treatment and management of influenza Part II: Future compounds against influenza virus. Journal of preventive medicine and hygiene. 2014;55(4):109.
56. Mousavi SM, Hashemi SA, Salahi S, Hosseini M, Amani AM, Babapoor A. Development of Clay Nanoparticles Toward Bio and Medical Applications. Current Topics in the Utilization of Clay in Industrial and Medical Applications. 2018;9:167.
57. Kaiser L, Wat C, Mills T, Mahoney P, Ward P, Hayden F. Impact of oseltamivir treatment on influenza-related lower respiratory tract complications and hospitalizations. Archives of internal medicine. 2003;163(14):1667-72.
58. Hsu J, Santesso N, Mustafa R, Brozek J, Chen YL, Hopkins JP, et al. Antivirals for treatment of influenza: a systematic review and meta-analysis of observational studies. Annals of internal medicine. 2012;156(7):512-24.
59. Doshi P, Jefferson T, Del Mar C. The imperative to share clinical study reports: recommendations from the Tamiflu experience. PLoS medicine. 2012;9(4).
60. Atapour A, Negahdaripour M, Ghasemi Y, Razmjuee D, Savardashtaki A, Mousavi SM, et al. In Silico Designing a Candidate Vaccine Against Breast Cancer. International Journal of Peptide Research and Therapeutics. 2019:1-12.
61. Khandaker G, Al Mamun A, Anovadiya AP, Araujo W, Azziz-Baumgartner E. Impact of neuraminidase inhibitors on influenza A (H1N1) pdm09-related pneumonia: an individual participant data meta-analysis. 2016.
62. Chen LF, Dailey NJ, Rao AK, Fleischauer AT, Greenwald I, Deyde VM, et al. Cluster of oseltamivir-resistant 2009 pandemic influenza A (H1N1) virus infections on a hospital ward among immunocompromised patients—North Carolina, 2009. Journal of Infectious Diseases. 2011;203(6):838-46.
63. Stephenson I, Democratis J, Lackenby A, McNally T, Smith J, Pareek M, et al. Neuraminidase inhibitor resistance after oseltamivir treatment of acute influenza A and B in children. Clinical Infectious Diseases. 2009;48(4):389-96.
64. Ramos EL, Mitcham JL, Koller TD, Bonavia A, Usner DW, Balaratnam G, et al. Efficacy and safety of treatment with an anti-m2e monoclonal antibody in experimental human influenza. The Journal of infectious diseases. 2015;211(7):1038-44.
65. Schotsaert M, De Filette M, Fiers W, Saelens X. Universal M2 ectodomain-based influenza A vaccines: preclinical and clinical developments. Expert review of vaccines. 2009;8(4):499-508.
66. Jegerlehner A, Schmitz N, Storni T, Bachmann MF. Influenza A vaccine based on the extracellular domain of M2: weak protection mediated via antibody-dependent NK cell activity. The Journal of Immunology. 2004;172(9):5598-605.
67. Mair-Jenkins J, Saavedra-Campos M, Baillie JK, Cleary P, Khaw F-M, Lim WS, et al. The effectiveness of convalescent plasma and hyperimmune immunoglobulin for the treatment of severe acute respiratory infections of viral etiology: a systematic review and exploratory meta-analysis. The Journal of infectious diseases. 2015;211(1):80-90.
68. Diaz E, Martin-Loeches I, Canadell L, Vidaur L, Suarez D, Socias L, et al. Corticosteroid therapy in patients with primary viral pneumonia due to pandemic (H1N1) 2009 influenza. Journal of Infection. 2012;64(3):311-8.
69. Brun-Buisson C, Richard J-CM, Mercat A, Thiébaut AC, Brochard L. Early corticosteroids in severe influenza A/H1N1 pneumonia and acute respiratory distress syndrome. American journal of respiratory and critical care medicine. 2011;183(9):1200-6.
70. Linko R, Pettilä V, Ruokonen E, Varpula T, Karlsson S, Tenhunen J, et al. Corticosteroid therapy in intensive care unit patients with PCR-confirmed influenza A (H 1 N 1) infection in F inland. Acta anaesthesiologica scandinavica. 2011;55(8):971-9.
71. Rodrigo C, Leonardi-Bee J, Nguyen-Van-Tam JS, Lim WS. Effect of corticosteroid therapy on influenza-related mortality: a systematic review and meta-analysis. The Journal of infectious diseases. 2015;212(2):183-94.
72. Zakeri A, Kouhbanani MAJ, Beheshtkhoo N, Beigi V, Mousavi SM, Hashemi SAR, et al. Polyethylenimine-based nanocarriers in co-delivery of drug and gene: a developing horizon. Nano reviews & experiments. 2018;9(1):1488497.
73. Kilbourne ED. Influenza immunity: new insights from old studies. The Journal of infectious diseases. 2006;193(1):7-8.
74. Glezen WP. Prevention and treatment of seasonal influenza. New England Journal of Medicine. 2008;359(24):2579-85.
75. Ang LW, Tien WS, Lin RTP, Cui L, Cutter J, James L, et al. Characterization of influenza activity based on virological surveillance of influenza-like illness in tropical Singapore, 2010–2014. Journal of medical virology. 2016;88(12):2069-77.
76. Zhao B, Qin S, Teng Z, Chen J, Yu X, Gao Y, et al. Epidemiological study of influenza B in Shanghai during the 2009–2014 seasons: implications for influenza vaccination strategy. Clinical Microbiology and Infection. 2015;21(7):694-700.
77. Kalkowska DA, Tebbens RJD, Pallansch MA, Cochi SL, Wassilak SG, Thompson KM. Modeling undetected live poliovirus circulation after apparent interruption of transmission: implications for surveillance and vaccination. BMC infectious diseases. 2015;15(1):66.
78. Zimmerman RK, Nowalk MP, Chung J, Jackson ML, Jackson LA, Petrie JG, et al. 2014–2015 influenza vaccine effectiveness in the United States by vaccine type. Clinical Infectious Diseases. 2016:ciw635.
79. Ohmit SE, Petrie JG, Malosh RE, Fry AM, Thompson MG, Monto AS. Influenza vaccine effectiveness in households with children during the 2012–2013 season: assessments of prior vaccination and serologic susceptibility. The Journal of infectious diseases. 2015;211(10):1519-28.
80. Flannery B, Clippard J, Zimmerman RK, Nowalk MP, Jackson ML, Jackson LA, et al. Early estimates of seasonal influenza vaccine effectiveness—United States, January 2015. MMWR Morbidity and mortality weekly report. 2015;64(1):10.
81. Li T, Chan MC, Lee N. Clinical implications of antiviral resistance in influenza. Viruses. 2015;7(9):4929-44.
82. Avval ZM, Malekpour L, Raeisi F, Babapoor A, Mousavi SM, Hashemi SA, et al. Introduction of magnetic and supermagnetic nanoparticles in new approach of targeting drug delivery and cancer therapy application. Drug Metabolism Reviews. 2019:1-28.
83. Merritt T, Hope K, Butler M, Durrheim D, Gupta L, Najjar Z, et al. Effect of antiviral prophylaxis on influenza outbreaks in aged care facilities in three local health districts in New South Wales, Australia, 2014. Western Pacific surveillance and response journal: WPSAR. 2016;7(1):14.
84. Louie JK, Salibay CJ, Kang M, Glenn-Finer RE, Murray EL, Jamieson DJ. Pregnancy and severe influenza infection in the 2013–2014 influenza season. Obstetrics & Gynecology. 2015;125(1):184-92.
85. Tech JET. Investigating the Activity of Antioxidants Activities Content in Apiaceae and to Study Antimicrobial and Insecticidal Activity of Antioxidant by using SPME Fiber Assembly Carboxen/Polydimethylsiloxane (CAR/PDMS). Journal of Environmental Treatment Techniques. 2020;8(1):214-24.