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(REVIEW ARTICLE)

Is H3N2 Influenza flare-up and troubling like COVID?

Raghavendra Rao M.V [1,*], Hitesh Lakshmi Billa [2], A. Rekha [3], Sireesha Bala [4], Mahendra Verma [5], M. M. Karindas [6], Ilie Vasiliev [7], Mallem Dinakar [8] and Chennamchetty Vijay Kumar [9]

[1] *Scientist-Emeritus, Director research, Apollo Institute of Medical Science and Research, Hyderabad, TS, India*
[2] *Department of Interventional Pulmonology, Apollo Institute of Medical Science and Research, Hyderabad, TS, India.*
[3] *Department of Surgery and Dean, Apollo Institute of Medical Sciences and Research, Jubilee Hills, Hyderabad, Telangana, India.*
[4] *Department of Pharmacology, Dean of Basic Medical sciences, Avalon University school of Medicine, Curacao.*
[5] *American University School of medicine, Aruba, Caribbean Islands.*
[6] *Department of Oncology, world Academy of Medical sciences, Netherlands.*
[7] *Department of Internal Medicine, world Academy of Medical sciences, Netherlands.*
[8] *Department of forensic Medicine, Apollo Institute of Medical, Sciences and Research, Jubilee Hills, Hyderabad, Telangana, India.*
[9] *Department of Pulmonary Medicine, Apollo Institute of Medical Science and Research, Hyderabad, TS, India.*

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Abstract

COVID and H3N2 influenza instances are on ascent in India. Both COVID-19 and H3N2 are the infectious viruses. They promulgate through droplets. COVID is transmitted by SARs –Cov2 virus and H3N2 acquired by Influenza A sub type. Contrast to H3N2, COVID 19 cause more serious and symptoms can take longer than flu symptoms. The COVID-19 not only poses a serious threat to the health of people worldwide but also affects the global economy. H3N2 is a variety of influenza virus that has been present among humans since the late 1960s. It is often called the "Hong Kong flu" due to its roots in Asia. Viruses that normally disperse in pigs are “swine influenza viruses". H3N2 is a subtype of the viral genus Influenza Virus A, which is a major cause of current respiratory illness. The H3N2 virus is a non-human influenza virus that normally circulates in pigs and has infected humans with symptoms similar to seasonal flu viruses. Influenza outbreaks have caused widespread illness to humans many times throughout history. In 1968 an avian reasserting virus of the H3N2 subtype was introduced into the human population that caused a global pandemic associated with more than one million deaths world-wide. About half of all inpatient severe acute respiratory infections.H3N2 hospitalized patients suffer from fever, cough, breathlessness and wheezing. Few patients needed oxygen and ICU care. Despite significant advancement in vaccine and virus research, influenza continues to be a major public health concern.

Keywords: Swine influenza viruses; Hemagglutinin (H); Neuraminidase (N); Poly-N-acetyl-lactosamine (poly-LacNAc) chains

1. Introduction

Influenza is a respiratory illness that infects between 5–15% of the global population annually. (1)

Those suffering from an influenza infection commonly display symptoms such as fever, sore throat, coughing, nasal discharge, headache, and myalgia. (2)

* Corresponding author: Raghavendra Rao M.V

In 1968 an avian reassortant virus of the H3N2 subtype was introduced into the human population that caused a global pandemic associated with more than one million deaths world-wide.(3)

More recently in 2009 an influenza pandemic caused by a novel strain of H1N1 resulted in millions of infections in more than 214 countries (4)

H3N2 influenza viruses have undergone extensive genetic and antigenic evolution (5)

Influenza A virus subtype H3N2 (A/H3N2) is a subtype of viruses that causes influenza (flu). H3N2 viruses can infect birds and mammals. (6)

Its name derives from the forms of the two kinds of proteins on the surface of its coat, hemagglutinin (H) and neuraminidase (N). By reassortment, H3N2 exchanges genes for internal proteins with other influenza subtypes (7)

Since the protective ability of influenza vaccines depends primarily on the closeness of the match between the vaccine virus and the epidemic virus, the presence of nonreactive H3N2 SIV variants suggests current commercial vaccines might not effectively protect pigs from infection with a majority of H3N2 viruses (8).

H3N2 evolved from H2N2 by antigenic shift and caused the Hong Kong Flu pandemic of 1968 and 1969 that killed up to 750,000 humans (9)

The WHO estimates that these infections result in 250,000–500,000 deaths every year (10)

The Influenza A(H3N2) virus caused many outbreaks and was responsible for the 1968 pandemic. During this pandemic, genetic re-assortment happened in the avian influenza virus, which caused millions of deaths worldwide, when got introduced in the human population (11)

The influenza virus is classified into 4 types (A, B, C and D) of which influenza A and B cause illness but influenza A, a member of *Orthomyxoviridae* family, causes pandemic. Influenza A is further classified into different subtypes based on the presence of hemagglutinin and neuraminidase surface antigen. (12)

From 2001 to 2002, the affinity reduced for an avian receptor but regained in 2003 the ability to bind with α-2,3 sialylated glycans prefer to bind with avian receptors (13)

Genome-wide analysis of 286 Influenza A (H3N2) viruses, the rate of mutation is more for surface antigens (hemagglutinin, neuraminidase) and PB1-F2 proteins (14)

Another study reported local fitness landscape for the antigenic binding site (B), one of the five binding sites (A–E) that also form a part of receptor-binding sites. (15)

Since 1968, numerous changes have occurred in the Influenza A(H3N2) virus genetically and antigenically through antigenic drift. (16)

The new substitutions affected its neutralization activity and helped in escaping from humoral immunity by gaining additional *N*-glycosylation site, at position 45 and 144(17)

Influenza A (H3N2) virus has maintained the human-type specificity, but has shifted their preference to receptors consisting of extended poly-*N*-acetyl-lactosamine (poly-LacNAc) chains. (18)

The infected patient produces ultrafine aerosol particles having a live virus that was proved in a study in which samples were collected by air samplers (19)

H3N2 is more severe than H1N1 in the case of C-reactive protein, fever, and leukopenia-type diseases and in a study, it is proved that H3 is more immunogenic than H1 (20)

2. History

The 1968 pandemic was caused by an influenza A (H3N2) virus comprised of two genes from an avian influenza A virus, including a new H3 hemagglutinin, but also contained the N2 neuraminidase from the 1957 H2N2 virus. It was first noted in the United States in September 1968.

Influenza A H3N2 variant viruses (also known as "H3N2v" viruses) with the matrix (M) gene from the 2009 H1N1 pandemic virus were first detected in people in July 2011. The viruses were first identified in U.S. pigs in 2010.

Both the H2N2 and H3N2 pandemic flu strains contained genes from avian influenza viruses. The new subtypes arose in pigs coinfected with avian and human viruses and were soon transferred to humans.

2.1. Types of influenza

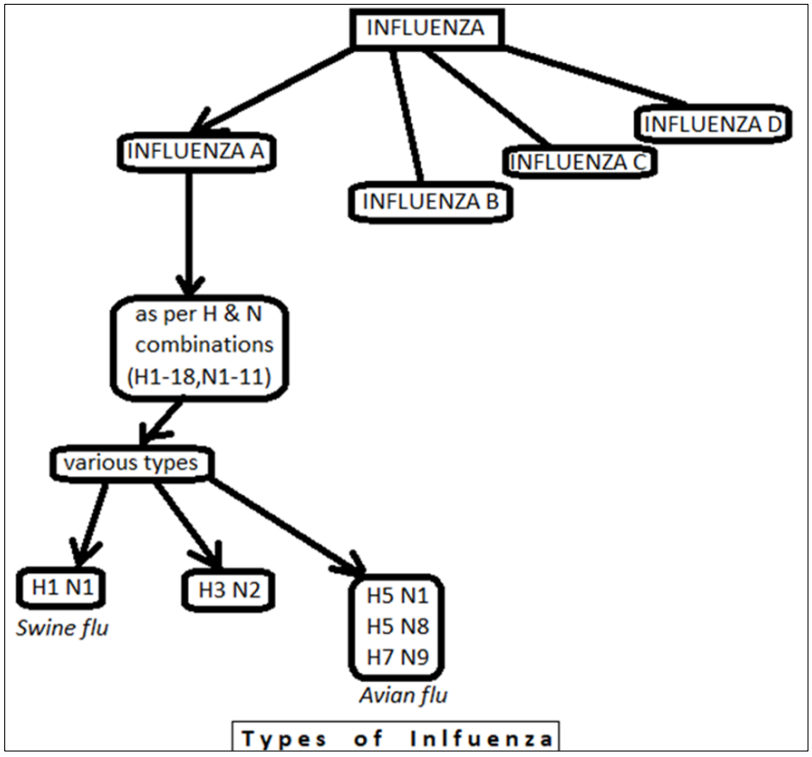

Figure 1 Types of influenza

3. Viral replication

Once the viral RNPs have been released they are directed into the host nucleus with the help of viral localization signals. (21)

In the nucleus, negative sense viral RNA is transcribed into positive sense mRNA using viral polymerase. The polymerase snatches 5′ caps from cellular RNA and 3′ RNA is polyadenylated in order to make viral pre-mRNA (22)

Also synthesized from the viral RNA is complementary RNA that RNA polymerase uses to transcribe more copies of negative–sense genome viral RNA allowing the virus to efficiently replicate its genetic material. (23)

Once the viral mRNA is capped and polyadenylated it is ready to be exported out of the nucleus and translated into proteins by the host ribosomes. The newly assembled proteins are then transported to the apical side of the cell membrane where the virions are assembled.

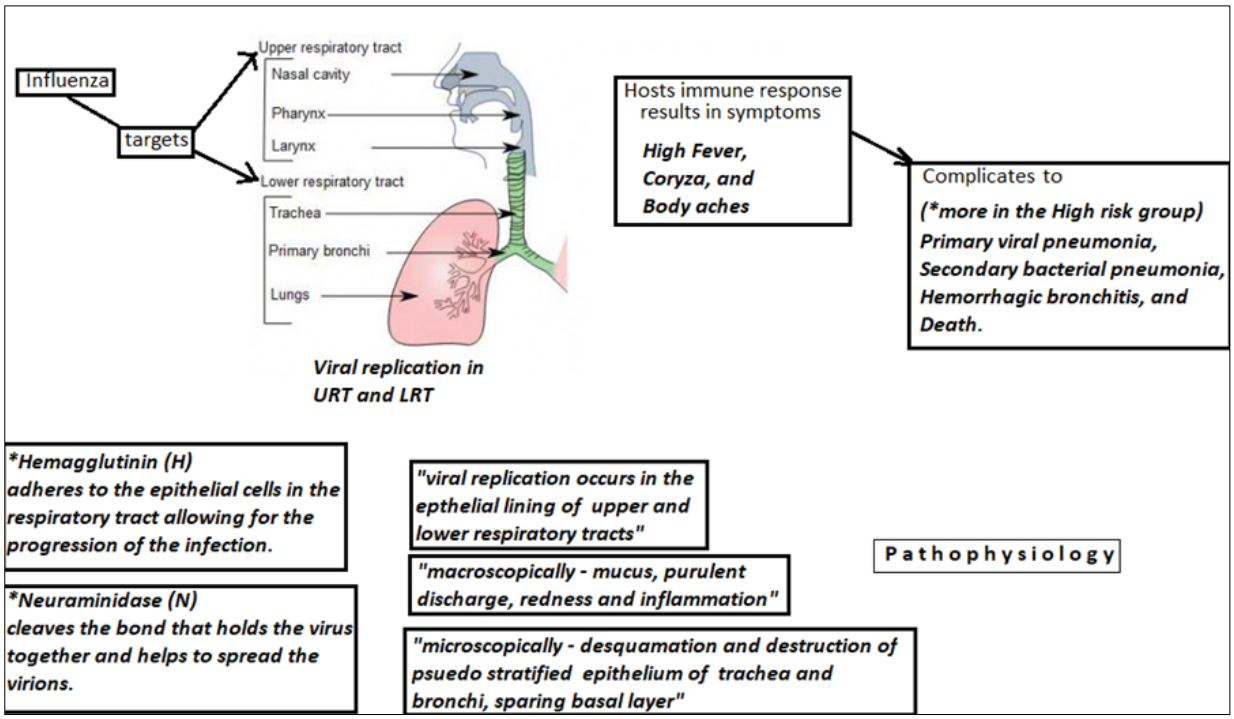

Figure 2 Viral Replication

4. Influenza---Symptomatology

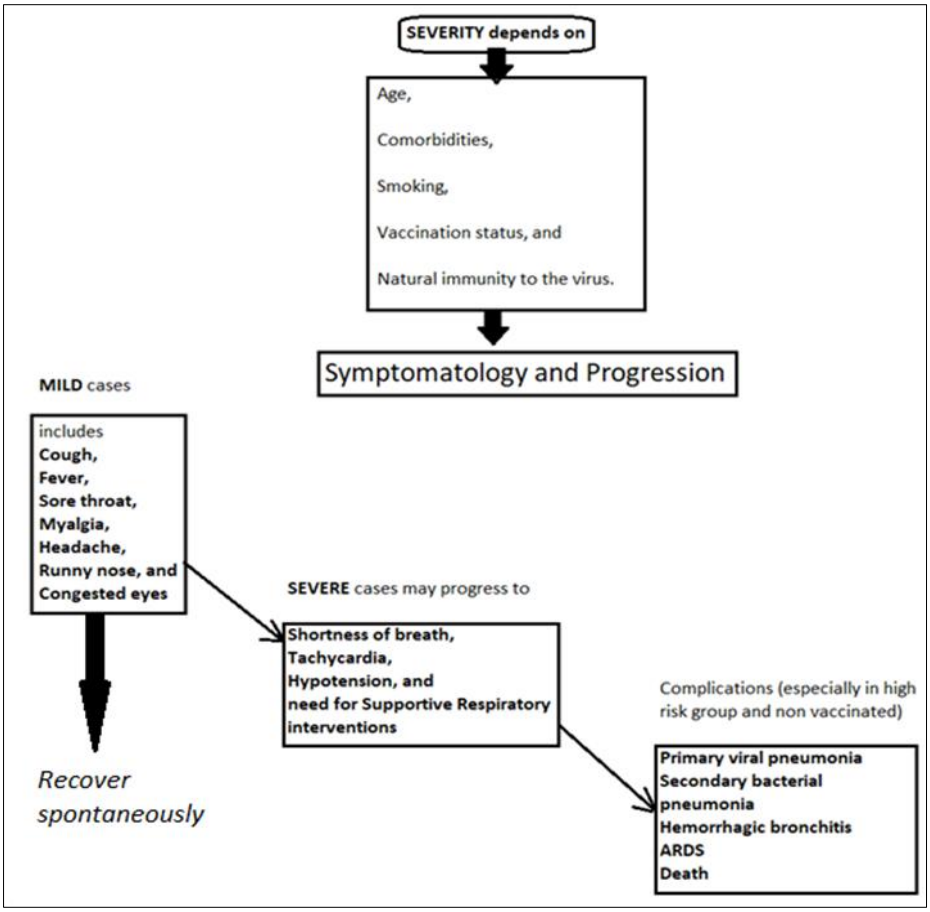

Figure 3 Symptomatology

Runny or stuffy nose, Sore throat with cough, Headache, Fever, Chills, Body ache, Fatigue and Diarrhoea are the common symptoms.

In mild cases, cough, fever sore throat myalgia, head ache, and runny nose are the common symptoms. In severe cases SOB, tachycardia, Hypotension, and need for supportive respiratory interventions. While there are no known side effects of the H3N2 virus on the kidneys, complications like acute kidney injury can happen, especially in patients on dialysis. Vaccination and good hygiene are the best ways to prevent infection

5. COVID and 2 H3N2 Active Reported in Jharkhand, So Far

In Jharkhand, there are now 10 confirmed cases of COVID-19 and two confirmed cases of H3N2. The H3N2 virus was discovered in its first case in Jamshedpur, and on Sunday, Ranchi reported the second case.

In the first instance, a 68-year-old woman who was confirmed to have the virus is now being treated at Tata Main Hospital. The district surveillance department has isolated her and her four family members at home and obtained samples after her reports came back positive.(24)

In the second instance, a young girl who has the flu is receiving treatment at a Ranchi private hospital. According to doctors, she is receiving oxygen therapy for her condition. In the state, 23% of residents have not yet received the second dose of the COVID vaccine. (25)

5.1. H3N2: The tiny monster

Dr. Tarun Sahani, senior consultant in internal medicine at Apollo Hospitals, said that just 5% of instances had been found to require hospitalization.Virologist Upasana Ray, a former member of the Indian National Young Academy of Science (INYAS) and the Global Young Academy (GYA), said everything should be alright if most affected persons recover. Long-term lockdowns and mask wear helped slow the spread of more dangerous virus strains but also limited exposure to seasonal respiratory viruses.

Dr. Anurag Agrawa, dean of Trivedi School of Biosciences at Ashoka University, stated that H3N2 is more severe than typical flu. The Integrated Disease Surveillance Program (IDSP) network allows the Union Health Ministry to monitor the seasonal influenza status in various states and UTs in real time.(26)

5.2. Andhra Pradesh state government to conduct door-to- door Influenza A detection

The Andhra Pradesh state government will conduct a door-to-door fever survey to find early-stage Influenza A illnesses and administer the required care.

The leading cause of the rise in viral fever is that people disregarded the COVID-19 standards. Individuals need to practice basic hygiene. Dr. Koka Mohana, a physician in Vijayawada, advised people to wash their hands frequently and use masks to protect themselves from viruses.(27)

5.3. Flu Incidences in Delhi-NCR are on the Rise Due to The H3n2 Virus

Dr. Amitabh Parti, director of internal medicine at Fortis Memorial Research Institute in Gurugram, noted that more than 40% of viral fever episodes at present are caused by the H3N2 virus. He added that after the acute viral infection subsides in the patient, they might experience spasms, shortness of breath, a chronic dry cough, and heaviness in the chest due to an immunological response in the airways of the lungs.

Dr. Virender Yadav, Gurugram's top medical officer, stated that at present there is undoubtedly an increase in viral cases, but that a majority of patients can recover within a week.

According to Dr. Kuldeep Kumar Grover, director of critical care at the CK Birla Hospital in Gurugram, they observe a spike in viral infections during January and February every year. The bulk of people impacted by the infection are under 15 and over 50 years old, and they frequently complain of fever in addition to upper respiratory diseases. (28)

6. Diagnosis

Traditional methods, e.g., viral culture serological methods, e.g., immunofluorescence assays, complement fixation, immunodiffusion test, virus neutralization method, hemagglutination method, rapid antigen testing.

6.1. Cell culture

The culturing of the virus was started in the 1940s and is considered to be the oldest conventional and recommended method for the diagnosis of influenza to study antigen characterization of new strains (29)

The embryonated eggs or mammalian cells are used for the propagation of the influenza virus for its recovery from clinical samples. In this method, the infectious samples are inoculated into the embryonated eggs or permissive cell lines and followed by one-week propagation (up to 10 days). The cytopathic effect is observed, and virus infection is checked by different methods, such as using immunofluorescence microscopy and molecular methods (30) This viral isolation technique is usually executed on formerly established cell lines, such as A549, rhesus monkey kidney (LLC MK2), Madin Darby canine kidney (MDCK), buffalo green monkey kidney (BGMK), and mink lung epithelial cell line (Mv1Lu), or primary cell lines, such as African green monkey kidney (AGMK) or rhesus monkey kidney (RhMK). (31)

MDCK cells have both α2,6 and α2,3-linked SA receptors and allow both avian and human influenza viruses to be cultured from this cell line with high HA titers (hemagglutination). Nevertheless, during the past years, a favorable binding of Influenza A(H3N2) virus isolates to α2,6-linked SA molecule has been observed (32,33)

Serological methods are generally used to diagnose antibodies response against the influenza virus. The serological tests include hemagglutination inhibition assay (HAI), virus neutralization assay (VN) or microneutralization, single radial hemolysis (SRH), complement fixation assay, enzyme-linked immunoabsorbent assay (ELISA), and Western blotting (34)

Enzyme-linked immunoassay (ELISA) ELISA tests are accessible for the diagnostic purpose since the 1990s that possesses high specificity and sensitivity (35)

Nucleic acid tests (NAT) employ PCR and virus-specific RNA or DNA sequences/genetic material instead of viral antibodies or antigens. Different NATs are accessible for influenza virus detection in humans, and these tests include nucleic acid sequencing-based amplification (NASBA), reverse transcriptase PCR (RT-PCR), loop-mediated isothermal amplification-based assay (LAMP), transcription-mediated amplification.

Biosensing techniques are the most recent development in the identification and diagnosis of the virus.(36)

7. FDA approves first combination test: "Lucira COVID-19 & Flu Home test"

The FDA approved the "Lucira COVID-19 & Flu Home test", the first COVID-19 and flu combo test which can be done at home and help people to determine the cause of a runny nose easily.

The combo test uses self-collected nasal swab samples, which is available without a prescription and produce results in roughly 30 minutes.

This is the first at-home test for influenza A and B, also known as the flu, despite home COVID tests being widely accessible. An emergency use authorization for the test was given, facilitating the accessibility of "medical counter-measures" during public health emergencies.

The FDAs Centre for Devices and Radiological Health director, Jeff Shuren, hailed the authorization as a significant step towards enhancing consumer access to diagnostic procedures that can be completed fully at home.The test is for those with symptoms and signs consistent with a respiratory tract infection. Additionally, it can be performed on children as young as two, with adults collecting the samples.

The FDA advises that tests be reported to healthcare professionals and warns about the possibility of misleading positive and negative results. The FDA asserted that it recognizes the advantages that home testing may offer and would endeavor to expand the number of tests accessible, keeping in mind the hazardous effects of COVID-19, RSV, and other respiratory infections. (37)

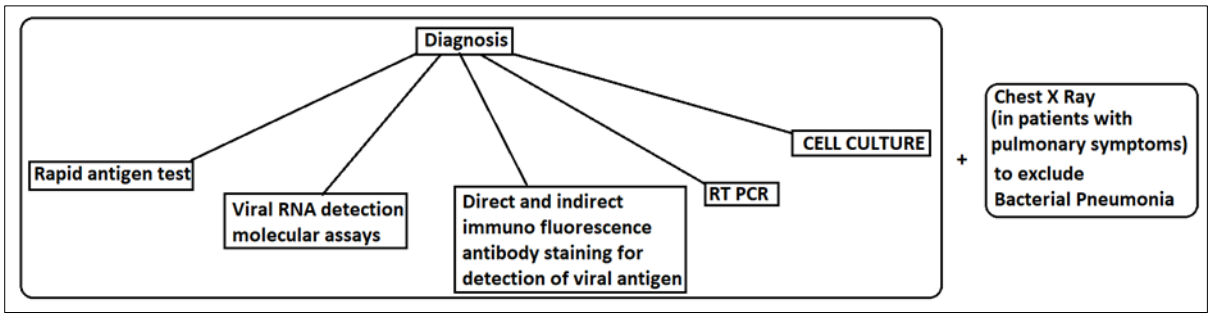

Figure 4 Diagnosis

8. Antivirals

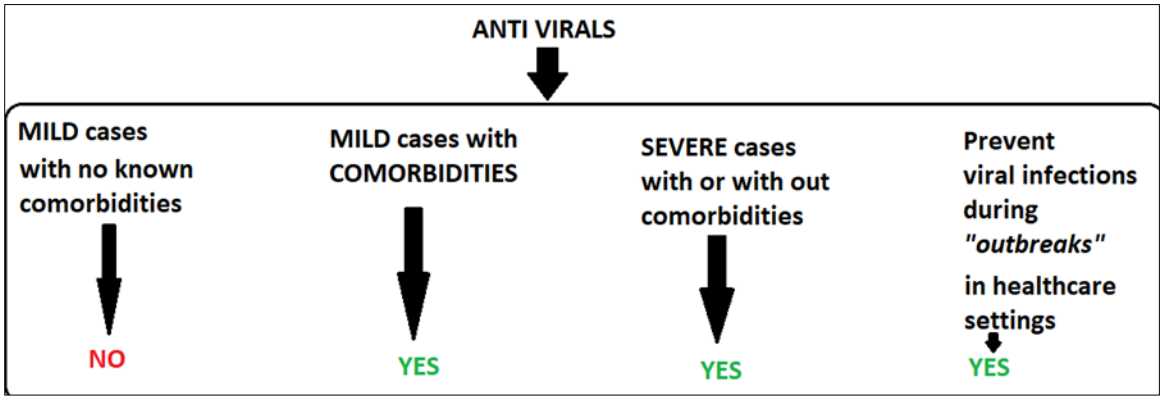

Figure 5 Antivirals

9. Treatment

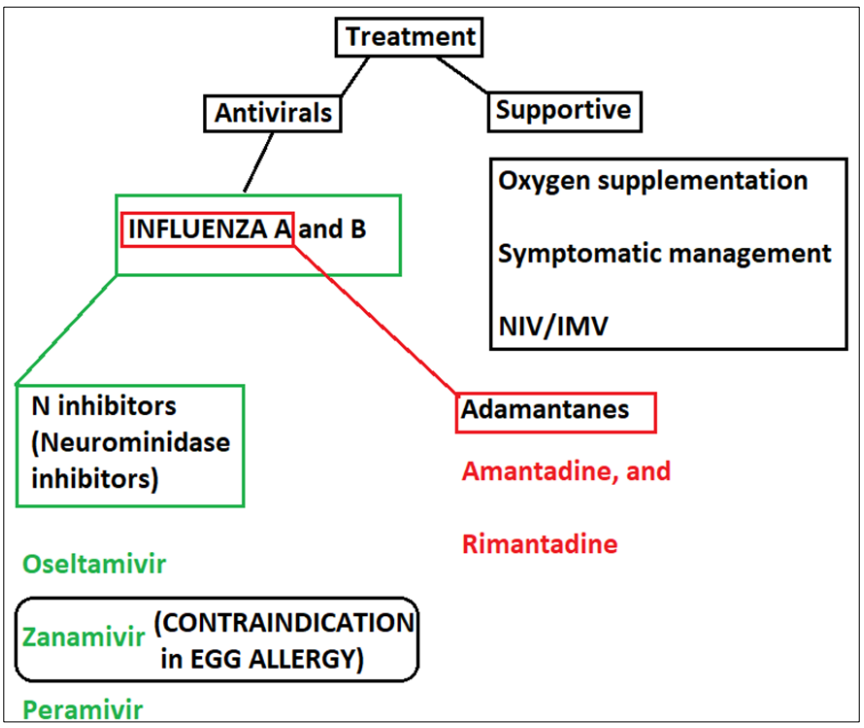

Figure 6 Treatment

For COVID 19 no drugs and other therapeutics are approved by FDA. Investigational treatments are available.Treatment for H3N2 influenza includes rest, drinking plenty of fluids, and taking over-the-counter medications such as acetaminophen or ibuprofen to reduce fever and relieve pain. Antiviral medications like oseltamivir and zanamivir may also be prescribed by a doctor for people with severe symptoms or those who are at high risk of complications. Oxygen supplementation is supportive.

10. Influenza vaccination

10.1. Bharat Biotech Working on H3N2 Vaccine Amid Surging Viral Cases

Dr. Krishna Ella, Founder Chairman of Bharat Biotech, stated that the company is currently working on an H3N2 vaccine amid the influenza virus in the country.

He added that a more effective H1N1 vaccine was developed by Bharat Biotech in 2015. H1N1 is also known as swine flu and is a subtype of the influenza A virus that causes respiratory infections. Early in March of this year, India experienced its first fatalities due to the influenza A subtype H3N2.

Earlier, the company had stated that it will be developing an antigen bank of 10 million doses as a stockpile for its COVID-19 nasal vaccine, iNOVACC. iNCOVACC, a recombinant, replication-deficient adenovirus vectored vaccine, was developed by the company in collaboration with Washington University in St. Louis. On the other hand, the inactivated virus intramuscular injectable vaccine Covaxin was developed by the company in collaboration with the Indian Council of Medical Research—National Institute of Virology (ICMR—NIV).(38)

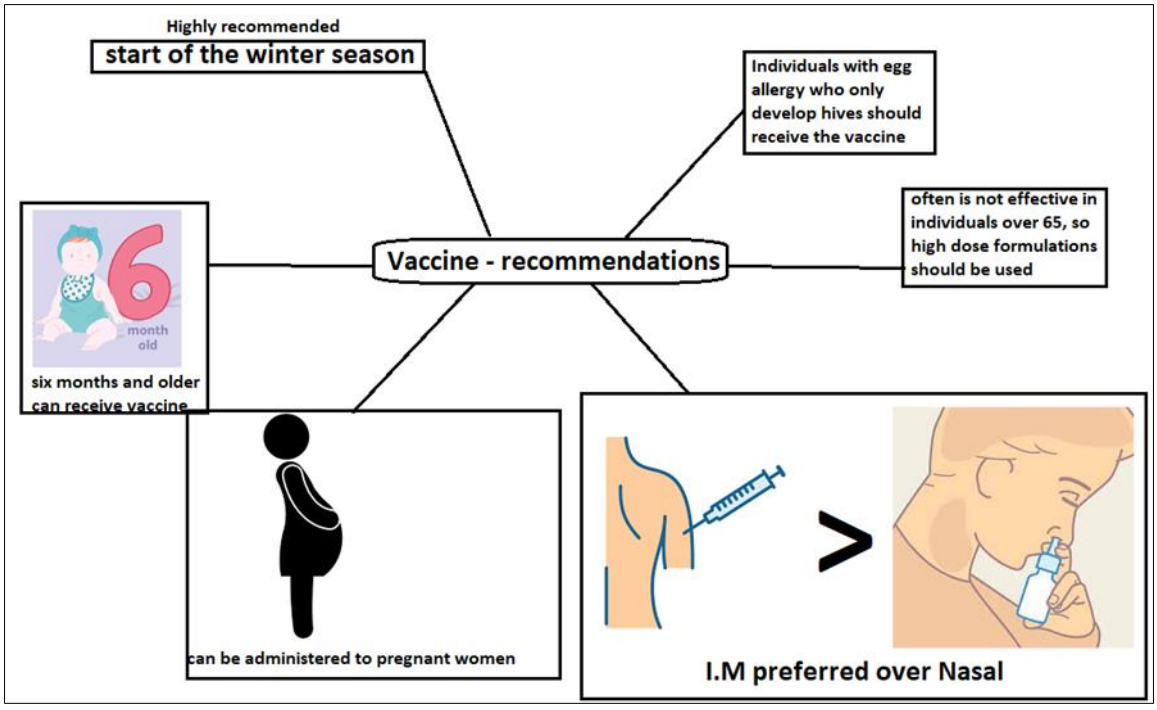

Figure 7 Vaccine recommendation

A prerequisite of production and supply of an optimal influenza vaccine is the selection and development of optimal candidate vaccine viruses, and the development and availability of vaccine potency reagents.

Two technologies are being used for the development of suitable candidate reassortant vaccine viruses:

Classical assortment, available since 1971 to generate hybrid viruses.

Reverse genetics, a patented technology, available to attenuate highly pathogenic viruses and reassort the attenuated HA and NA with backbone virus.

Reference antigen and sheep antisera are developed by ERLs in collaboration with vaccine manufacturers, standardized by ERLs, and made available to manufacturers worldwide on request.

11. Prophylaxis

11.1. How to prevent it from spreading? Precautions important rather than worrying

Washing hands before eating or touching your face, nose or mouth, carrying pocket sanitiser, and avoiding people already infected with the virus or any other seasonal flu are some of the steps one can take to make sure they don't fall sick due to the H3N2 infection. Moreover, a healthy diet that includes plenty of fruits and vegetables can also play a significant role in improving immunity. The doctor added that drinking a lot of fluids, and eating home-cooked, low-spice and low-fat food can also help.

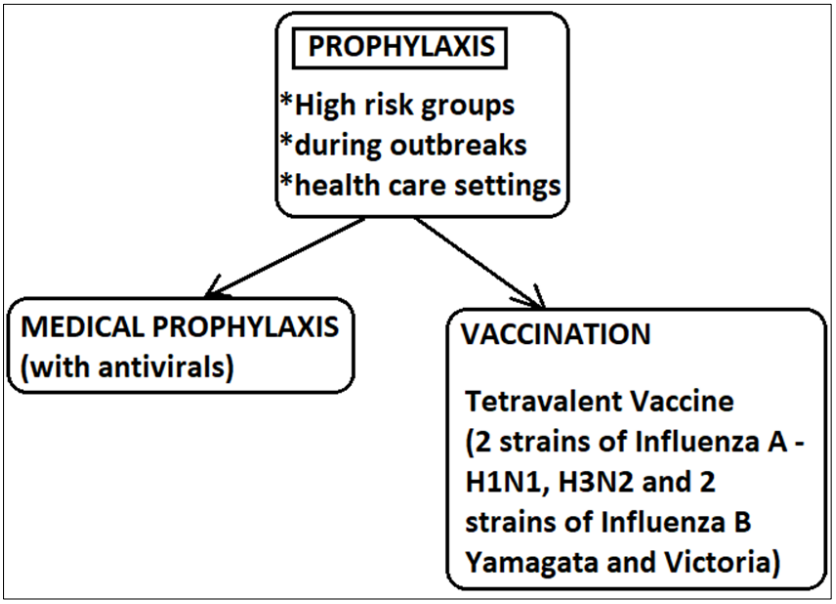

Figure 8 Prophylaxis

11.2. Update on Seasonal Influenza

Union Health Ministry monitoring and tracking cases across States through the IDSP network on real-time basis. Cases of H3N2 subtype of Seasonal Influenza being strictly monitored. Advisories issued by ICMR on Precautions for Prevention. Union Health Ministry is keeping a close watch on the Seasonal Influenza situation in various States/UTs through the Integrated Disease Surveillance Programme (IDSP) network on real-time basis. The Ministry is also tracking and keeping a close watch on morbidity and mortality due to the H3N2 subtype of the seasonal Influenza. Young children and old age persons with co-morbidities are the most vulnerable groups in context of seasonal influenza

12. Conclusion

The non-human influenza virus H3N2v mostly infects pigs but has also infected people. Viruses known as "swine influenza viruses" typically infect pigs. These viruses are known as "variant" viruses when they infect humans. A particular H3N2 virus with genes from avian, swine, and human viruses as well as the M gene from the 2009 H1N1 pandemic virus was discovered in 2011. In 2010 the virus was present in pigs, and it wasn't until 2011 that it was discovered in humans. This virus may infect people more quickly than usual for other swine influenza viruses as a result of acquiring the 2009 M gene. Similar to seasonal flu viruses, H3N2v infections can cause fever, respiratory symptoms like cough and runny nose, as well as other symptoms including body aches, nausea, vomiting, or diarrhea.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors have no conflicts of interest to declare.

References

[1] Vemula SV, Zhao J, Liu J, Wang X, Biswas S, Hewlett I. Current approaches for diagnosis of influenza virus infections in humans. Viruses. 2016, 8(4):96. doi: 10.3390/v8040096. PMID:27077877. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[2] Shim JM, Kim J, Tenson T, Min JY, Kainov DE. Influenza Virus Infection, Interferon Response, Viral Counter-Response, and Apoptosis. Viruses. 2017, 9(8):223. doi: 10.3390/v9080223. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[3] Alymova IV, York IA, Air GM, Cipollo JF, Gulati S, Baranovich T, Kumar A, Zeng H, Gansebom S, McCullers JA. Glycosylation changes in the globular head of H3N2 influenza hemagglutinin modulate receptor binding without affecting virus virulence. Scientific Rep. 2016, 6:36216. [PMC free article] [PubMed] [Google Scholar]

[4] Yang J, Liu S, Du L, Jiang S. A new role of neuraminidase (NA) in the influenza virus life cycle: implication for developing NA inhibitors with novel mechanism of action. Rev Med Virology. 2016, 26(4):242–50. doi: 10.1002/rmv.1879. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[5] Lin Y, Wharton SA, Whittaker L, Dai M, Ermetal B, Lo J, Pontoriero A, Baumeister E, Daniels RS, McCauley JW. The characteristics and antigenic properties of recently emerged subclade 3C. 3a and 3C. 2a human influenza A (H3N2) viruses passaged in MDCK cells. Influenza Other Respir Viruses. 2017, 11(3):263–74. doi: 10.1111/irv.12447. PMID: 28164446. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[6] "Pink Book | Influenza | Epidemiology of Vaccine Preventable Diseases | CDC". CDC. 2019-03-29. Retrieved 6 June 2019. Greater number of hospitalizations during years that A(H3N2) is predominan

[7] Marozin, S., Gregory, V., Cameron, K., Bennett, M., Valette, M., Aymard, M., Foni, E., Barigazzi, G., Lin, Y., Hay, A.YR 2002 (2002). "Antigenic and genetic diversity among swine influenza A H1N1 and H1N2 viruses in Europe". Journal of General Virology. 83 (4): 735–745. doi:10.1099/0022-1317-83-4-735.

[8] René Gramer, Marie, Hoon Lee, Jee, Ki Choi, Young, Goyal, Sagar M., Soo Joo, Han (2007). "Serologic and genetic characterization of North American H3N2 swine influenza A viruses". Canadian Journal of Veterinary Research. 71 (3): 201–206. .

[9] WHO (28 October 2005). "H5N1 avian influenza: timeline" (PDF). Archived from the origin on 27 July 2011.

[10] Vemula SV, Zhao J, Liu J, Xue XW, Biswas HSI (2016) Current approaches for diagnosis of influenza virus infections in humans. Viruses 8:1–15

[11] Shim JM, Kim J, Tenson T, Min JY, Kainov DEV (2017) Counter-response, influenza virus infection, interferon response, viral counter-response, and apoptosis. Viruses 9:223.

[12] Influenza update 362, 2020. https://www.who.int/influenza/surveillance_monitoring/updates/latest_update_GIP_surveillance/en/. Accessed on 2 Mar 2020

[13] Wang YY, Harit D, Subramani DB, Arora H, Kumar PA, Lai SK (2017) Influenza-binding antibodies immobilise influenza viruses in fresh human airway mucus. Eur Respir J 49:160–170

[14] Westgeest KB, Russell CA, Lin X, Spronken MIJ, Bestebroer TM, Bahl J, Van Beek R, Skepner E, Halpin RA, De Jong JC, Rimmelzwaan GF, Osterhaus ADME, Smith DJ, Wentworth DE, Fouchier RAM, Graaf D (2014) Genomewide analysis of reassortment and evolution of human influenza A (H3N2) viruses circulating between 1968 and 2011. J Virol 88:2844–2857.

[15] Wu NC, Otwinowski J, Thompson AJ, Nourmohammad A, Wilson IA, Nycholat CM (2020) Major antigenic site B of human influenza H3N2 viruses has an evolving local fitness landscape. Nat Commun 11:1–10

[16] Lin C, Guo Y, Zhao M, Sun M, Luo F, Guo L, Qiu B, Lin Z, Chen G (2017) Highly sensitive colorimetric immunosensor for influenza virus H5N1 based on enzyme-encapsulated liposome. Anal ChimActa 963:112–118.

[17] Ushirogawa H, Naito T, Tokunaga H, Tanaka T, Nakano T, Terada K (2016) Re-emergence of H3N2 strains carrying potential neutralizing mutations at the N-linked glycosylation site at the hemagglutinin head, post the 2009 H1N1 pandemic. BMC Infect Dis 16:380.

[18] Peng W, de Vries RP, Grant OC, Thompson AJ, McBride R, Tsogtbaatar B, Lee PS, Razi N, Wilson IA, Woods RJ, Paulson JC (2017) Recent H3N2 viruses have evolved specificity for extended, branched human-type receptors, conferring potential for increased avidity. Cell Host Microbe 21:23–34.

[19] Lednicky JA, Loeb JC (2013) Detection and isolation of airborne influenza A H3N2 virus using a Sioutas personal cascade impactor sampler. Influenza Res Treat 2013:656825.

[20] Treanor JJ, Schiff GM, Couch RB, Cate TR, Brady RC, Hay CM, Wolff M, She D, Cox MM (2006) Dose-related safety and immunogenicity of a trivalent baculovirus-expressed influenza-virus hemagglutinin vaccine in elderly adults. J Infect Dis. 193:1223–1228.

[21] Yang J, Liu S, Du L, Jiang S. A new role of neuraminidase (NA) in the influenza virus life cycle: implication for developing NA inhibitors with novel mechanism of action. *Rev Med Virology*. 2016, 26(4):242–50. doi: 10.1002/rmv.1879

[22] Shim JM, Kim J, Tenson T, Min JY, Kainov DE. Influenza Virus Infection, Interferon Response, Viral Counter-Response, and Apoptosis. Viruses. 2017, 9(8):223. doi: 10.3390/v9080223

[23] Bouvier NM and Palese P. The biology of influenza viruses. Vaccine. 2008, 26:D49–53. doi: 10.1016/j.vaccine.2008.07.039. PMID:19230160

[24] https://www.daijiworld.com/news/newsDisplay?newsID=1062168

[25] The Hindu,March 10, 2023 05:27 pm | Updated March 15, 2023 01:24 pm IST - New Delhi

[26] https://health.economictimes.indiatimes.com/news/industry/increase-precaution-no-need-to-panic-experts-as-india-records-two-h3n2-virus-deaths/98560440)

[27] https://timesofindia.indiatimes.com/city/vijayawada/door-to-door-survey-to-detect-influenza-a/articleshow/98465253.cms

[28] https://health.economictimes.indiatimes.com/news/hospitals/h3n2-virus-is-causing-spike-in-flu-cases-in-delhi-ncr-doctors/97937573

[29] McMullen AR, Anderson NW, Burnham CAD, Education Committee of the Academy of Clinical Laboratory Physicians and Scientists Pathology consultation on influenza diagnostics. Am J ClinPathol. 2016, 145(440):448

[30] Vemula SV, Zhao J, Liu J, Xue XW, Biswas HSI. Current approaches for diagnosis of influenza virus infections in humans. Viruses. 2016, 8:1–15.

[31] Chambers BS, Li Y, Hodinka RL, Hensley SE. Recent H3N2 influenza virus clinical isolates rapidly acquire hemagglutinin or neuraminidase mutations when propagated for antigenic analyses. J Virol. 2014, 88:10986–10989.

[32] Parker L, Wharton SA, Martin SR, Cross K, Lin Y, Liu Y, Feizi T, Daniels RS, McCauley JW. Effects of egg-adaptation on receptor-binding and antigenic properties of recent influenza A (H3N2) vaccine viruses. J Gen Virol. 2016, 97:1333–1344.

[33] Yang H, Carney PJ, Chang JC, Guo Z, Villanueva JM, Stevens J. Structure and receptor binding preferences of recombinant human A (H3N2) virus hemagglutinins. Virology. 2015, 477:18–31.

[34] Le TT, Chang P, Benton DJ, McCauley JW, Iqbal M, Cass AE. Dual recognition element lateral flow assay toward multiplex strain specific influenza virus detection. Anal Chem. 2017, 89(12):6781–6786

[35] Leirs K, Tewari KP, Decrop D, Pérez-Ruiz E, Leblebici P, Van Kelst B, Compernolle G, Meeuws H, Van Wesenbeeck L, Lagatie O, Stuyver L. Bioassay development for ultrasensitive detection of influenza a nucleoprotein using digital ELISA. Anal Chem. 2016, 88:8450–8458

[36] Kumar N, Bhatia S, Pateriya AK, Sood R, Nagarajan S, Murugkar HV, Kumar S, Singh P, Singh VP. Label-free peptide nucleic acid biosensor for visual detection of multiple strains of influenza A virus suitable for field applications. Anal Chim Acta. 2020, 1093:123–130.

[37] https://www.tribuneindia.com/news/world/fda-authorises-combination-flu-COVID-test-for-home-use-482986

[38] https://health.economictimes.indiatimes.com/news/pharma/amid-rising-viral-cases-bharat-biotech-working-on-h3n2-vaccine/98748236 a