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Research Article

Seasonal Influenza in Morocco

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Abstract

Influenza is an acute respiratory infection caused by influenza viruses of the Orthomyxoviridae family. Influenza virus cell culture consists of inoculating viral isolates on an MDCK cell layer. The objective of this work is to describe the role of cell culture in influenza virus subtyping during the 2023/2024 influenza epidemic at the Mohammed V Military Teaching Hospital - Rabat.

This is a prospective descriptive study carried out at the Virology laboratory of the HMIMV in Rabat, during the 2023/2024 influenza epidemic season (between October and May). It included all samples from patients positive for influenza viruses by the respiratory PCR test. Of the 86 samples positive by PCR, 36 were selected for viral culture.

Cell culture allowed the isolation of the virus from the original sample, thus producing a sufficient quantity for further antigenic and genetic characterization, allowing the subtyping of circulating strains.

The results showed a predominance of influenza A(H3N2) with 35 cases out of 36 compared to influenza A(H1N1) pdm09 with only 1 case.

Cell culture also makes it possible to assess the sensitivity of isolated viral strains to antiviral molecules and to detect the emergence of resistance. Thus, it plays an important role in virological surveillance and in alerting to the event of the appearance of new viruses.

More Information

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Keywords: Influenza; Flu; Epidemic; Pandemic; Cell culture

Introduction

Influenza is a contagious acute respiratory infection caused by Influenza viruses of the Orthomyxoviridae family, which are enveloped viruses with segmented, single-stranded RNA of negative polarity.

The history of influenza is marked by several pandemics and virus mutations that have affected global health. The Spanish flu pandemic in 1918 was the most devastating in modern history, caused by the A(H1N1) virus, which infected around a third of the world's population and killed 50 million people [1,2].

The 1957 Asian pandemic caused by the A(H2N2) virus, considered clinically milder than that of the A(H1N1) virus, was responsible for around 1.1 million deaths worldwide [3]. The 1968 Hong Kong pandemic caused by the A(H3N2) virus, derived from H2N2, was responsible for around 1 million deaths. This A(H3N2) virus is still circulating nowadays in mutated forms [4]. The pandemic of 2009, caused by a new variant of the A(H1N1) subtype, resulted in around 284,400 deaths worldwide [5,6].

According to new estimates published by the WHO in 2023, there will be around one billion cases of seasonal influenza each year, including 3 to 5 million severe cases, and between 290,000 and 650,000 respiratory-related deaths [7].

Diagnosis of influenza is based primarily on clinical assessment, taking into account the epidemiological context. In severe cases, in patients at risk or in epidemic situations [1], virological diagnosis is carried out using rapid tests, 1st-line antigenic screening tests [8], or molecular biology techniques such as "multiplex" PCR [9]. Treatment combines symptomatic and antiviral approaches, notably neuraminidase

inhibitors (oseltamivir, zanamivir) [8] and new molecules such as baloxavir marboxil [9]. Other avenues of research are exploring monoclonal antibodies against resistant strains [10]. Although influenza vaccines are available and effective [11], ongoing viral mutations mean that their composition needs to be updated annually [12].

Cell culture enables the isolation and identification of different circulating viral strains, the detection of antigenic and genetic mutations in emerging viruses, and the formulation of seasonal vaccines. Cell culture also assesses the sensitivity of isolated viral strains to antiviral molecules. As such, it plays an important role in virological surveillance and in warning of the emergence of new viruses [13,14].

Since January 1, 2023, the highly pathogenic avian influenza virus A(H5N1) has caused 261 human cases, including 142 deaths, for a mortality rate of 54% [15], raising major public health concerns due to its high lethality despite low morbidity and human-to-human transmission, justifying rigorous global surveillance to prevent a pandemic with potentially devastating consequences [16].

This work aims to describe the virological aspects of the 2023/2024 influenza epidemic at the Mohammed V Military Teaching Hospital of Rabat.

Materiel and methods

Type of study

This is a prospective study conducted at the cell culture unit of the Virology Laboratory of the Mohammed V Military Teaching Hospital of Rabat, over the period of the 2023/2024 influenza epidemic season (from 01/10/2023 to 30/05/2024).

Inclusion criteria

The specimens included in our study correspond to samples sent to the virology laboratory for respiratory virus testing in patients presenting with influenza-like illness from all departments of the Mohammed V Military Teaching Hospital.

The study included all specimens from patients positive for influenza viruses using the multiplex respiratory PCR test, targeting the simultaneous detection of several circulating viruses: influenza viruses (Influenza A and B), SARS-CoV-2, and respiratory syncytial virus (RSV).

Of the 86 PCR-positive samples, 36 were selected for viral culture, presenting a fairly high viral load determined by a Ct < 34 (Table 1).

Table 1: Threshold PCR amplification cycle (Ct) for selected samples.

Sample no.	1	2	3	4	5	6	7	8	9	10	11	12
Ct	33	27	29	25	24	27	19	31	22	32	25	28
Sample no.	13	14	15	16	17	18	19	20	21	22	23	24
Ct	26	24	25	28	22	31	31	24	23	28	28	27
Sample no.	25	26	27	28	29	30	31	32	33	34	35	36
Ct	26	26	25	27	26	22	24	30	28	29	30	31

Samples and techniques for virological diagnosis

Samples: Nasal and/or oropharyngeal swabbing involves collecting cells from the upper respiratory tract, in compliance with recommended protective measures.

The sample must be transported to the laboratory as quickly as possible at room temperature. After the processing protocol, the sample is stored at -80 °C for subsequent studies, as in the case of our work.

Virological diagnostic techniques: Cepheid®'s Xpert® Xpress Cov-2/Flu/RSV plus respiratory multiplex PCR test simultaneously amplifies four specific viral targets: Influenza viruses (A and B), SARS-CoV-2, and Respiratory Syncytial Virus.

This test has been used for virological diagnosis of all samples from people suspected of having a respiratory viral infection, and delivers rapid results within 36 min (Table1).

The results obtained enable the simultaneous detection and differentiation of specific target genes for SARS-CoV-2, influenza A virus, influenza B virus, and RSV in clinical samples. However, the test is not designed to detect the influenza C virus. These results do not exclude the possibility of bacterial infection or co-infection with other pathogens not detected by the test [17].

Culture of PCR-positive samples

Processing positive samples for influenza virus isolation: When good-quality clinical samples are available, viral isolation is a highly sensitive and useful method for diagnosing viral infection. One of the main advantages of this technique is that it amplifies the amount of virus present in the initial sample, generating a sufficient quantity for in-depth antigenic and genotypic analysis, as well as for antiviral susceptibility testing if required [15].

First, vortex the swab and transport medium, then add 0.2 ml of gentamicin solution (50 mg/ml) to one milliliter of transport medium. Leave at room temperature for 15 minutes and centrifuge at 1000 rpm for 5 minutes, finally remove the supernatant and use 200 µl for virus isolation to prepare a 1:2 dilution.

Preparation of MDCK cell suspension: MDCK (Madin-Darby Canine Kidney) cells are a cell line derived from canine kidney cells, used in influenza virus research for their ability to infect and replicate the virus. They are used to identify and quantify virus infectivity, as well as for the production of viruses for vaccines and the study of viral infection mechanisms [16].

The procedure used a 12-well (P-12) plate with a confluent MDCK cell monolayer [15] with D-MEM (Dulbecco's Modified Eagle's Medium), incubated at 37 °C.

Inoculation of cell cultures: Influenza virus inoculation involves introducing the viral suspension onto laboratory-grown MDCK cells to induce infection and allow virus replication. All steps must be carried out in a class II Microbiological Safety Cabinet (MSC) to prevent contamination of the cells.

The MDCK cells must be healthy and in a monolayer with a confluence of 70% - 95%. Using an inverted optical microscope, the D-MEM medium from the plates and the cells were washed with MEM (Minimum Essential Medium) basal medium, then 200 µL of each treated sample was inoculated, with its 1/2 dilution, into P-12 plates (Figures 1,2).

For virus isolation, the cells must not be in the growth phase; therefore, everything that is not essential for survival is removed from the D-MEM medium (growth factors, vitamins, glucose, etc.).

Cell control wells allow monitoring of cell evolution without any viral sample.

The sample adsorbs to the cells for 30 minutes at 37 °C. We added 6 ml of MEM medium for cell maintenance containing 2 µg/ml of TPCK-trypsin to the plates. Then incubate at 35 °C and observe daily for the appearance of the cytopathic effect.

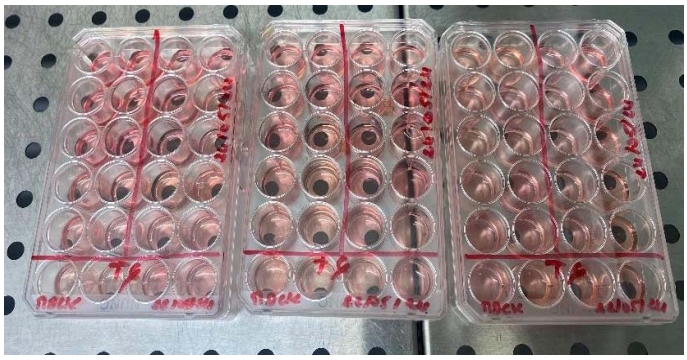

Figure 1: P-24 plates with MDCK cells ready for viral isolation (photo taken at the virology laboratory, HMIMV-Rabat).

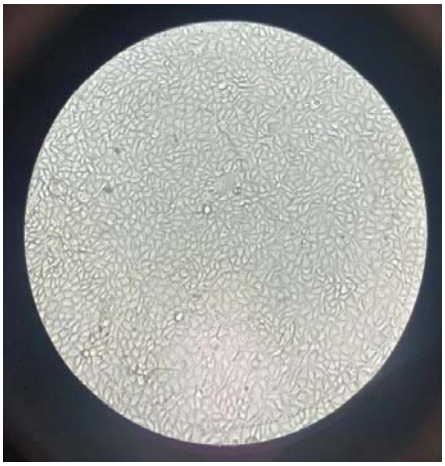

Figure 2: MDCK cell seen under an inverted microscope (x20 objective) (photo taken at the virology laboratory, HMIMV-Rabat).

Viral isolation: Viral isolation is a process used to obtain live viral particles for subsequent quantification, genetic analysis of strains, or research into new antiviral molecules or vaccines.

The viral suspension is recovered when a cytopathic effect is observed; otherwise, recovery takes place on day 6, and the isolated virus is stored at -80 °C for subsequent studies.

Detection of viral isolates

Observed cytopathic effect: The cytopathic effect (CPE) refers to all metabolic, biochemical, and morphological alterations in a host cell infected by viruses. Viral replication mobilizes a large proportion of the cell's biochemical resources, resulting in profound changes that vary according to the type of virus. This effect can manifest itself in different ways: cell rounding and retraction, cell lysis, and release of virions (Table 2).

Hemagglutination test: The hemagglutination test is used to determine the hemagglutination titer of viral strains. The influenza virus contains numerous hemagglutinin (HA) molecules on its surface. HA is a protein that specifically binds to sialic acid-containing receptors such as those found on the plasma membrane of red blood cells (RBCs). When RBCs are mixed with the influenza virus in the appropriate proportions, the virus binds to the RBCs and alters their normal sedimentation pattern. This is called hemagglutination [15].

For this test, the WHO recommends the use of chicken, turkey, guinea pig, or human type O RBCs because they have receptor analogs and a high concentration of sialic acid required for binding to viral hemagglutinin [18]. We used human type O-negative RBCs for this test. The highest dilution of virus that causes complete hemagglutination is considered the endpoint of the hemagglutination titration. Hemagglutination occurs when red blood cells remain in suspension after the red blood cell marker has completely settled (Figure 3, Table 3).

Identification of viral isolates using the hemagglutination inhibition assay (HAI)

Identification, also known as subtyping, of influenza viruses

Table 2: Onset time of cytopathic effects (CPE) in days.

Sample no.	1	2	3	4	5	6	7	8	9	10	11	12
PCE onset time (days)	5	5	5	4	3	4	3	5	2	5	4	4
Sample no.	13	14	15	16	17	18	19	20	21	22	23	24
PCE onset time (days)	3	3	4	5	4	5	5	4	3	5	5	5
Sample no.	25	26	27	28	29	30	31	32	33	34	35	36
PCE onset time (days)	3	4	4	5	5	4	5	5	5	5	5	5

Table 3: Hemagglutination titre of samples.

Sample no.	1	2	3	4	5	6	7	8	9	10	11	12
HA Titre	4	8	4	8	8	8	4	8	16	8	4	4
Sample no.	13	14	15	16	17	18	19	20	21	22	23	24
HA Titre	4	8	4	8	8	8	8	4	4	4	4	8
Sample no.	25	26	27	28	29	30	31	32	33	34	35	36
HA Titre	4	8	4	4	4	8	4	4	4	8	4	4

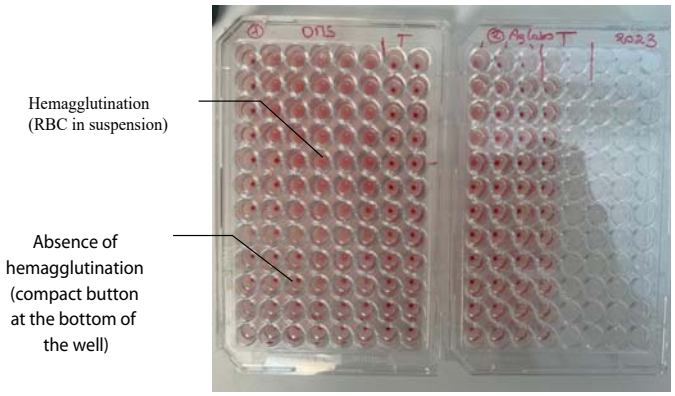

Figure 3: P-96 plates for the hemagglutination test (photo taken at the virology laboratory, HMIMV).

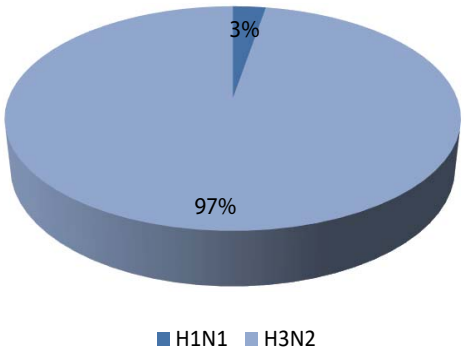

Figure 4: Graph of the identification results of the different influenza strains isolated at HMIMV-Rabat in 2023/2024.

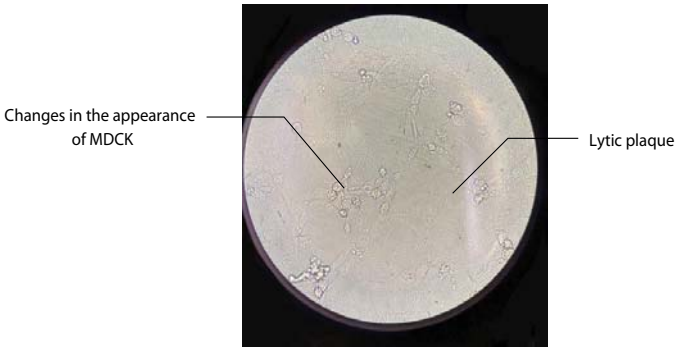

Figure 5: Cytopathic effects of the A H3N2 virus seen under an inverted microscope (40x objective) (Photo taken at the virology laboratory, HMIMV-Rabat).

can be carried out using the hemagglutination inhibition assay (HAI), which exploits specific interactions between antibodies and hemagglutinin (HA) proteins present on the virus surface.

In the HAI assay, antibodies specific to different HA subtypes (H1, H3) are added to a mixture containing our viral isolate and RBCs. The specific binding of the antibody to antigenic sites on the HA molecule interferes with the binding between the viral HA protein and receptors on the RBC membrane. This effect inhibits hemagglutination and forms the basis of the test. A viral isolate is identified as a particular subtype if it reacts with the corresponding antiserum: the antigen-antibody reaction occurs, and hemagglutination of RBCs is inhibited. Results are interpreted to identify the virus subtype on the basis of the HAI titre obtained, which corresponds to the inverse of the highest dilution of antiserum that completely inhibits hemagglutination. The HAI test is the test of choice for global influenza surveillance and analysis of the antigenic characteristics of viral isolates [19,20].

To perform this test, we used WHO-produced antisera, prepared in goats by multiple intramuscular injections with purified HA from reference influenza strains. These antisera enable the identification of influenza viruses of type A(H3N2), A(H1N1)pdm09, and type B (Victoria and Yamagata lines) in human influenza isolates (Table 4). The results of the HAI test of our 36 samples showed a predominance of influenza A(H3N2) with 35 cases out of 36 or 97% compared to influenza A(H1N1)pdm09 with only 1 case or 3% (Figures 4,5).

The low hemagglutinating power observed in our cell cultures is mainly due to the predominance of influenza A(H3N2) compared to influenza A(H1N1); in fact, the highest hemagglutinating titer obtained (Table 3) was observed in sample no. 9, corresponding to the A(H1N1) strain.

Table 4: Hemagglutination inhibition test.

Sample no.	1	2	3	4	5	6	7	8	9
Identification of influenza A subtypes	H3N2	H3N2	H3N2	H3N2	H3N2	H3N2	H3N2	H3N2	H1N1
Sample no.	10	11	12	13	14	15	16	17	18
Identification of influenza A subtypes	H3N2	H3N2	H3N2	H3N2	H3N2	H3N2	H3N2	H3N2	H3N2
Sample no.	19	20	21	22	23	24	25	26	27
Identification of influenza A subtypes	H3N2	H3N2	H3N2	H3N2	H3N2	H3N2	H3N2	H3N2	H3N2
Sample no.	28	29	30	31	32	33	34	35	36
Identification of influenza A subtypes	H3N2	H3N2	H3N2	H3N2	H3N2	H3N2	H3N2	H3N2	H3N2

Discussion

There are four types of influenza viruses: A, B, C, and D. Influenza A and B viruses cause seasonal epidemics and even pandemics for type A, while type C viruses generally cause mild, sporadic infections with no risk of widespread spread [21]. Type D viruses exclusively affect cattle and do not cause known diseases in humans [22].

Type A viruses can be classified based on the antigenic variation of the HA and NA antigens. So far, 16 HA variants and 9 NA variants have been identified; several HA and NA combinations are possible as subtypes [21]. The virus attaches to the host respiratory cell and penetrates the membrane. Hemagglutinin (HA) is a viral glycoprotein that binds to sialic acid expressed on the cell surface and initiates viral entry. Neuraminidase (NA) is a viral enzyme that aids in replication and allows the virus to release from the host cell after its viral multiplication cycle [21].

This viral infection is mostly mild, characterized by the following symptoms: fever, fatigue, headache, myalgia, and

bronchitis, but can lead to serious complications such as pneumonia, sepsis, especially in people with underlying pathologies, as well as infants and young children [21,23].

Seasonal epidemics occur every winter between October and May for the northern hemisphere, including Morocco, and between April and September for the southern hemisphere [24].

In Morocco, seasonal epidemics are documented in the epidemiological bulletin of the Moroccan Ministry of Health and Social Protection, published in April 2024. A short-term influenza epidemic spread over 15 weeks was noted, with an epidemic peak in week S3 and low activity of influenza viruses with a positivity rate of 12.7%. The 245 positive tests for influenza among the 1925 samples received at Moroccan surveillance laboratories confirmed a majority circulation of influenza A(H3N2) viruses compared to that of influenza A(H1N1)pdm09 during the 2023/2024 season. That of influenza B is almost absent, with a positivity proportion of 0.4% [23]. These national results are consistent with our preliminary results, which showed a majority identification of influenza A(H3N2) with 35 out of 36 cases, or 97%, compared to influenza A(H1N1)pdm09 with only 1 case, or 3%.

The duration, activity, and intensity of the 2023/2024 influenza season were similar in Morocco, Europe, and North America. According to data from the annual epidemiological report published by the European Centre for Disease Prevention and Control (ECDC), the 2023-2024 influenza season was a short season, with 15 weeks of sentinel positivity above the 10% threshold. Overall, influenza A(H1N1) pdm09 viruses were dominant in samples from sentinel and non-sentinel sources, from both primary and secondary care [25-27]. According to the Centers for Disease Control and Prevention (CDC) 2023/2024 influenza season review, the severity of the influenza season was classified as moderate, and influenza activity returned to levels observed in seasons before the COVID-19 pandemic [28].

According to the WHO Global Influenza Surveillance and Response System (GISRS), influenza activity recorded globally during the 2023/2024 season remained high in most countries in the Northern Hemisphere, while in the temperate zones of the Southern Hemisphere, influenza activity indicators were reported at low to medium levels in most countries. Influenza A viruses predominated, particularly A(H3N2), followed by A(H1N1) pdm09. For influenza B viruses, only the Victoria subtype was detected during this season [29]. These epidemiological data, antigenic characterization, and other genetic data were used at the WHO meeting on influenza vaccine composition in February 2024, during which recommendations were formulated for the 2024/2025 influenza season in the Northern Hemisphere [30]. Two commercial influenza vaccines are available on the Moroccan market: Influvac Tetra®, an inactivated surface antigen vaccine, and Vaxigrip Tetra®, an inactivated split virus vaccine. Both vaccines are obtained from viruses inoculated into embryonated chicken eggs [31]. For the 2023/2024 flu season, the Sanofi laboratory, which produces its Vaxigrip Tetra® vaccine, has distributed 400,000 doses, of which 150,000 doses are intended for the public market (Institut Pasteur du Maroc, Ministry of Health, etc.) and 250,000 others for the private market (wholesalers, distributors, community pharmacies, etc.). Sanofi's "Vaxigrip Tetra®" is presented in multidose for the public market via the Institut Pasteur du Maroc and in single-dose for the private market. The public sale price is 125.30 DH. It is also one of the medicines reimbursable under the Mandatory Health Insurance (AMO) [32].

Seasonal influenza vaccines are designed to protect against the four influenza viruses expected to circulate most widely during the upcoming season. Currently, three different influenza vaccine production technologies exist: egg-based vaccines, cell culture-based vaccines, and recombinant vaccines [33-35]. Currently, influenza vaccine production relies heavily on the use of embryonated chicken eggs. While this manufacturing method offers many advantages, such as achieving high influenza virus titers and experience with large-scale production, several drawbacks may affect its effectiveness. First, the adaptation of reassortant viruses in eggs prolongs the time required to produce influenza vaccines for the following influenza season. Some influenza strains (such as H3N2 viruses) are poorly cultured in eggs [36]. Several studies have demonstrated that the virus propagated in mammalian cell systems is structurally or antigenically identical to the field virus compared to that grown in embryonated chicken eggs [37,38]. According to several hypotheses, these adaptive mutations in eggs alter viral antigenicity and may therefore be partially responsible for lower vaccine efficacy [36,39].

In recent years, the use of cell culture has surpassed the use of embryonated eggs to isolate and culture influenza viruses and may become the predominant process for the development and production of future influenza vaccines [17]. This production method, approved by the Food and Drug Administration (FDA) in 2012, involves several steps. First, influenza viruses are grown on cell lines to produce candidate vaccine viruses (CVVs), which are then supplied to a vaccine manufacturer. This vaccine manufacturer inoculates CVVs into mammalian cells grown on an industrial scale and allows the CVVs to replicate.

Two licensed influenza vaccines are produced in the United States using cell culture: the recombinant vaccine grown in insect cells (RIV, Flublok®) and the inactivated vaccine grown in mammalian cells (ccIIV, Flucelvax®) [37].

Influenza viruses are constantly evolving, the emergence and spread of viruses resistant to antivirals is caused by

specific point mutations in the viral proteins targeted by current therapeutics, hence the urgency to evaluate the genetic and antigenic changes in the hemagglutinins (HA) of circulating viruses, to develop new active compounds and to closely monitor the resistance profiles of circulating influenza viruses in the international context [8]. These antigenic characterizations must be studied using the hemagglutination inhibition (HAI) test on strains isolated from cell culture [40]. This test also makes it possible to titrate the antibodies developed after vaccination, which makes it possible to evaluate vaccine efficacy in the population [41]. Cell culture also allows for monitoring of susceptibility to NA inhibitors among circulating influenza viruses worldwide [16]. According to the latest CDC publication in 2024, 6 cases of reduced effect of oseltamivir were detected out of a total of 5,163 viruses collected in the United States during the antiviral susceptibility study [40].

Cell culture allows for the isolation of the virus from the original sample, thus producing a sufficient quantity for further antigenic and genetic characterization, allowing for the subtyping of circulating strains, antiviral susceptibility testing, and the evaluation of vaccine efficacy. In recent years, the use of cell cultures has surpassed the use of embryonated eggs for the isolation and cultivation of influenza viruses [16].

Conclusion

The results of our study showed a predominance of influenza A(H3N2) during season 2023-2024, with97% of identified strains, compared to influenza A(H1N1) pdm09, with only3%. Influenza viruses are constantly evolving, and cell culture makes it possible to monitor sensitivity to antivirals and the potential emergence of resistance, as well as to assess the effectiveness of available vaccines by titrating antibodies developed after vaccination in the population. It therefore plays a very important role in virological surveillance and in warning of the emergence of new viruses.

References

1. Jester B, Uyeki TM, Jernigan DB, Tumpey TM. Historical and clinical aspects of the 1918 H1N1 pandemic in the United States. Virology. 2019;527:32–7. Available from: https://doi.org/10.1016/j.virol.2018.10.019
2. Johnson NPAS, Mueller J. Updating the accounts: global mortality of the 1918-1920 "Spanish" influenza pandemic. Bull Hist Med. 2002;76(1):105–15. Available from: https://doi.org/10.1353/bhm.2002.0022
3. Viboud C, Simonsen L, Fuentes R, Flores J, Miller MA, Chowell G. Global mortality impact of the 1957–1959 influenza pandemic. J Infect Dis. 2016;213(5):738–45. Available from: https://doi.org/10.1093/infdis/jiv534
4. Centers for Disease Control and Prevention (CDC). 1968 Pandemic (H3N2 virus) | Pandemic Influenza (Flu). 2024. Available from: https://archive.cdc.gov/www_cdc_gov/flu/pandemic-resources/1968-pandemic.html
5. Mena I, Nelson MI, Quezada-Monroy F, Dutta J, Cortes-Fernández R, Lara-Puente JH, et al. Origins of the 2009 H1N1 influenza pandemic in swine in Mexico. eLife. 2016;5:e16777. Available from: https://doi.org/10.7554/eLife.16777
6. Dawood FS, Reed C, Meltzer MI, Shay DK, Cheng PY. Estimated global mortality associated with the first 12 months of 2009 pandemic influenza A H1N1 virus circulation: a modelling study. Lancet Infect Dis. 2012;12(9):687–95. Available from: https://doi.org/10.1016/s1473-3099(12)70121-4
7. World Health Organization (WHO). Grippe saisonnière. 2024. Available from: https://www.who.int/fr/news-room/fact-sheets/detail/influenza-(seasonal)
8. Duwe S. Influenza viruses – antiviral therapy and resistance. GMS Infect Dis. 2017;5:Doc04. Available from: https://doi.org/10.3205/id000030
9. Kommandantvold SA, Lemenuel-Diot A, Skedgel C, Pitman R, Rouse P. A cost-effectiveness analysis of reduced viral transmission with baloxavir marboxil versus oseltamivir or no treatment for seasonal and pandemic influenza management in the United Kingdom. Expert Rev Pharmacoecon Outcomes Res. 2024;24(8):953–66. Available from: https://doi.org/10.1080/14737167.2024.2365421
10. Ison MG, Yoshida Y, Shishido T, Mitchener M. Early treatment with baloxavir marboxil in high-risk adolescent and adult outpatients with uncomplicated influenza (CAPSTONE-2): a randomised, placebo-controlled, phase 3 trial. Lancet Infect Dis. 2020;20(10):1204–14. Available from: https://doi.org/10.1016/s1473-3099(20)30004-9
11. Administrator. Vaccins antigrippaux. World Health Organization - Regional Office for the Eastern Mediterranean. 2024. Available from: http://www.emro.who.int/fr/health-topics/influenza/influenza-vaccines.html
12. Nuwarda RF, Alharbi AA, Kayser V. An Overview of Influenza Viruses and Vaccines. Vaccines. 2021;9(9):1032. Available from: https://doi.org/10.3390/vaccines9091032
13. Barer MR. Medical Microbiology. 2018. Available from: https://shop.elsevier.com/books/medical-microbiology/barer/978-0-7020-7200-0
14. Masson E. Culture cellulaire et virologie. Intérêts et applications de la culture cellulaire en virologie. EM-Consulte. 2024. Available from: https://www.em-consulte.com/article/263914/culture-cellulaire-et-virologie-interets-et-applic
15. World Health Organization. Manual for the laboratory diagnosis and virological surveillance of influenza. WHO Global Influenza Surveillance Network. 2011. Available from: https://iris.who.int/handle/10665/44518
16. Cai M, Gong Z, Dong T, Liu B, Su M, Li X. Production, Passaging Stability, and Histological Analysis of Madin–Darby Canine Kidney Cells Cultured in a Low-Serum Medium. Vaccines. 2024;12(9):Art. no. 9. Available from: https://doi.org/10.3390/vaccines12090991
17. [Xpert Xpress SARS-CoV-2 Flu RSV HC IVD FRENCH Package Insert 302-5707-FR Rev. A.pdf].
18. Gamblin SJ, Vachieri SG, Xiong X, Zhang J, Martin SR, Skehel JJ. Hemagglutinin Structure and Activities. Cold Spring Harb Perspect Med. 2021;11(10):a038638. Available from: https://doi.org/10.1101/cshperspect.a038638
19. Medeiros R, Escriou N, Naffakh N, Manuguerra JC, Van Der Werf S. Hemagglutinin Residues of Recent Human A(H3N2) Influenza Viruses That Contribute to the Inability to Agglutinate Chicken Erythrocytes. Virology. 2001;289(1):74–85. Available from: https://doi.org/10.1006/viro.2001.1121
20. Lin YP, Collins P, Kloess J, Wharton S, Cattle N. Neuraminidase Receptor Binding Variants of Human Influenza A(H3N2) Viruses Resulting from Substitution of Aspartic Acid 151 in the Catalytic Site: a Role in Virus Attachment? J Virol. 2010;84(13):6769–81. Available from: https://doi.org/10.1128/jvi.00458-10
21. Javanian M, Barary M, Ghebrehewet S, Koppolu V, Vasigala V, Ebrahimpour S. A brief review of influenza virus infection. J Med Virol. 2021;93(8):4638–46. Available from: https://doi.org/10.1002/jmv.26990
22. Liu R, Sheng Z, Huang C, Wang D, Li F. Influenza D virus. Curr Opin Virol. 2020;44:154–61. Available from: https://doi.org/10.1016/j.coviro.2020.08.004

23. World Health Organization (WHO). Influenza (Seasonal). 2024. Available from: https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal)

24. Zeno EE, Regan A, Couto P, Rondy M, Jara J, Voto C. Interim Effectiveness Estimates of 2024 Southern Hemisphere Influenza Vaccines in Preventing Influenza-Associated Hospitalization — REVELAC-i Network, Five South American Countries, March–July 2024. MMWR Morb Mortal Wkly Rep. 2024;73(39):861–8. Available from: https://doi.org/10.15585/mmwr.mm7339a1

25. Bedford T, Suchard MA, Lemey P, Dudas G, Gregory V, Hay AJ, et al. Integrating influenza antigenic dynamics with molecular evolution. arXiv. 2013. Available from: https://doi.org/10.48550/arXiv.1304.3637

26. [Epidemiological Bulletin for Influenza and Severe Acute Respiratory Infections, 2023-24 season.pdf].

27. Seasonal influenza, 2023-2024, Annual Epidemiological Report, 2023. Available from: https://www.ecdc.europa.eu/en/publications-data/seasonal-influenza-annual-epidemiological-report-20232024

28. Centers for Disease Control and Prevention (CDC). 2023-2024 Influenza Season Summary: Influenza Severity Assessment, Burden and Burden Prevented. 2024. Available from: https://www.cdc.gov/flu/whats-new/flu-summary-addendum-2023-2024.html

29. [flunetchart]. Available from: https://worldhealthorg.shinyapps.io/flunetchart/

30. Influenza virus characterization - Summary Europe, March 2024. Available from: https://www.ecdc.europa.eu/en/publications-data/influenza-virus-characterization-summary-europe-march-2024

31. Recherche de « Vaccins » - Medicament.ma. Available from: https://medicament.ma/?choice=classeTherapeutique&s=15229

32. Seasonal flu vaccine: 400,000 doses between the public and private markets in 2023. Le Matin.ma. 2024. Available from: https://lematin.ma/societe/vaccin-contre-la-grippe-400000-doses-entre-le-marche-public-et-prive/202359

33. Announcement of recommendations for the composition of the influenza vaccine for the 2023-2024 influenza season in the Northern Hemisphere. Available from: https://www.who.int/fr/news/item/24-02-2023-recommendations-announced-for-influenza-vaccine-composition-for-the-2023-2024-northern-hemisphere-influenza-season

34. Announcement of recommendations for the composition of influenza vaccines for the 2024-2025 influenza season in the Northern Hemisphere. Available from: https://www.who.int/fr/news/item/23-02-2024-recommendations-announced-for-influenza-vaccine-composition-for-the-2024-2025-northern-hemisphere-influenza-season

35. Centers for Disease Control and Prevention (CDC). How Influenza (Flu) Vaccines Are Made. 2024. Available from: https://www.cdc.gov/flu/vaccine-process/index.html

36. Skowronski DM, De Serres G, Sabaiduc S, Eshaghi A, Dickinson JA. Low 2012–13 Influenza Vaccine Effectiveness Associated with Mutation in the Egg-Adapted H3N2 Vaccine Strain Not Antigenic Drift in Circulating Viruses. PLoS One. 2014;9(3):e92153. Available from: https://doi.org/10.1371/journal.pone.0092153

37. Barr IG, Katz JM, McCauley JW, Odagiri T. Cell culture-derived influenza vaccines in the severe 2017–2018 epidemic season: a step towards improved influenza vaccine effectiveness. NPJ Vaccines. 2018;3(1):44. Available from: https://doi.org/10.1038/s41541-018-0079-z

38. Hegde NR. Cell culture-based influenza vaccines: A necessary and indispensable investment for the future. Hum Vaccin Immunother. 2015;11(5):1223–34. Available from: https://doi.org/10.1080/21645515.2015.1016666

39. Zost SJ, Gumina ME, Kim K, Diaz Perez S, Wilson PC. Contemporary H3N2 influenza viruses have a glycosylation site that alters binding of antibodies elicited by egg-adapted vaccine strains. Proc Natl Acad Sci USA. 2017;114(47):12578–83. Available from: https://doi.org/10.1073/pnas.1712377114

40. Centers for Disease Control and Prevention (CDC). Influenza Activity in the United States during the 2023–2024 Season and Composition of the 2024–2025 Influenza Vaccine. 2024. Available from: https://www.cdc.gov/flu/whats-new/flu-summary-2023-2024.html

41. Centers for Disease Control and Prevention (CDC). Antigenic Characterization. 2024. Available from: https://www.cdc.gov/flu/php/viruses/antigenic.html