

MONTHLY SCIENTIFIC REVIEW ON AVIAN INFLUENZA A (H5N1, H1N1, H3N2)

The content of this document is subject to change as the health situation evolves.
All informations comes from a valid and credible source.

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Situation at a glance

- On 29 March 2026, Cambodia reported its third human case of A(H5N1) of the year.
- In 2025, 18 human cases of A(H5N1) occurred in Cambodia, including 9 deaths, and 30 cases were reported globally. No human-to-human transmission has been identified.
- On 25 March, the first human case of A(H9N2) in Europe was reported in Italy, in a traveler returning from a non-European country.
- In late June, a case of avian influenza H5N1 was detected in a bird in Western Australia. This is the first time this H5 subtype (H5N1, clade 2.3.4.4b) has been identified in an animal in Australia.

Scientific articles

This section presents relevant articles published on peer-reviewed scientific journals or pre-print platforms.

2026-04-27

Effect of Acid-Stabilizing Hemagglutinin Mutations on Immunogenicity and Heterologous Protection by H1N1 Influenza Virus mRNA-LNP Vaccines.

Journal: Viruses

Authors: Chet R Ojha, Samuel W Rovito, Balaji Banoth, Hyunsuh Kim, Jeremy C Jones, Mohamad-Gabriel Alameh, Po-Ling Chen, Richard J Webby, Drew Weissman, Charles J Russell

Acid-stabilizing HA mutations K153E and K58I enhanced H1N1 mRNA-LNP vaccine immunogenicity, with K153E providing broader protection via increased HA expression, ASCs, and cross-reactive Tfh cells.

[See details](#)

2026-05-27

Emergence and Evolution of Triple Reassortant Highly Pathogenic Avian Influenza A(H5N1) Virus, Argentina, 2025.

Journal: Viruses

Authors: Estefania Benedetti, Maria Carolina Artuso, Alex Byrne, Maria de Belen Garibotto, Martín Avaro, Luana Piccini, Ariana Chamorro, Marcelo Sciorra, Vanina Marchione, Mara Russo, Maria Elena Dattero, Erika Macias Machicado, Monica Galiano, Nicola Lewis, Andrea Pontoriero

A novel triple reassortant H5N1 virus emerged in Argentina in 2025, combining Eurasian, North American, and South American lineages. Genomic analyses revealed potential mammalian adaptations, including HA substitutions and the I292M mutation in PB2. Phylogenetic studies s

[See details](#)

2026-05-27

Hypoxia-Enhanced N110 Glycosylation of Hemagglutinin Promotes H3N2 Influenza Virus Fitness by Modulating Receptor Binding and Immune Evasion.

Journal: Viruses

Authors: Ting Zhang, Yihui Fang, Jie Liu, Ao Guo, Bin Yuan, Yanan Zhang, Lihua Ding, Qinong Ye

Hypoxia boosts N110 glycosylation of H3N2 HA, enhancing viral fitness, pathogenicity, and immune evasion via B4GAT1-B4GALT1 complex. Vaccination with N110-containing HA offers broad protection.

[See details](#)

2026-05-12

Long noncoding RNA#61 synergizes with viral PA-X to augment pyroptosis and attenuate the virulence of highly pathogenic H5N1 influenza virus in mice.

Journal: J Virol

Authors: Xia Chen, Xinxin Zheng, Lei Zhang, Xinxin Cai, Xinping Hong, Siyu Hou, Xuran Ma, Zenglei Hu, Min Gu, Xiaoquan Wang, Ruyi Gao, Shunlin Hu, Yu Chen, Xiaowen Liu, Daxin Peng, Xiufan Liu, Jiao Hu

LncRNA#61, delivered via lipid nanoparticles, attenuates H5N1 influenza virus replication and virulence in mice by activating lipid metabolism, cell death, and mTORC1 pathways, enhancing GSDMD-mediated pyroptosis. Viral PA-X protein synergizes with LncRNA#61, promoting py

[See details](#)

2026-04-23

Serum-antibody profiling of H3N2-infected ferrets using a combinatorial phage-display random peptide library.

Journal: J Mol Biol

Authors: Tehila Yehudai, Gaik Tamazian, Lakshminarasaiah Uppalapati, Sandra Völs, Saranya Sridhar, Guadalupe Cortés, Thorsten U Vogel, Anna Roitburd-Berman, Jonathan M Gershoni

Motifier pipeline identified unique antibody signatures and infection-related peptide-motif markers in H3N2-infected ferrets, enabling accurate biological condition prediction.

[See details](#)

2026-05-16

H5N1 2.3.4.4b HA E190D and Q226H mutations, picked up as minority variants in a patient, result in an inability to bind sialic acid.

Journal: Virology

Authors: Eszter Kovács, María Ríos Carrasco, Mafalda F Guerreiro Cabana, Robert P de Vries

H5N1 2.3.4.4b HA E190D and Q226H mutations, found as minority variants in a patient, eliminate binding to avian- and human-type sialylated glycans, indicating impaired receptor-binding capacity across multiple H5 backgrounds.

[See details](#)

2026-04-30

Prior immunity to seasonal influenza A(H3N2) virus confers varying levels of cross-protection against challenge with clade 2.3.4.4b A(H5N1), A(H7N9), or A(H9N2) virus in a ferret model.

Journal: Microbiol Spectr

Authors: Xiangjie Sun, Jessica A Belser, Zhu-Nan Li, Feng Liu, Nicole Brock, Joanna A Pulit-Penalzo, Troy J Kieran, Claudia Pappas, Hui Zeng, Jessie C Chang, Paul J Carney, Brandon L Bradley-Ferrell, James Stevens, Min Z Levine, Terrence M Tumpey, Taronna R Maines

Prior A(H3N2) immunity in ferrets showed variable cross-protection against zoonotic IAVs, with some protection against A(H5N1) and A(H9N2), but minimal against A(H7N9), highlighting the unpredictable nature of cross-protection.

[See details](#)

2026-05-11

Computational Structural Analysis Predicts Host-Range Promiscuity and Antiviral Resistance in North American H5N1 Lineages.

Journal: Comput Struct Biotechnol J

Authors: Sayal Guirales-Medrano, Kary Ocaña, Khaled Obeid, Rachel Alexander, Colby T Ford, Daniel Janies

North American H5N1 (clade 2.3.4.4b) exhibits seasonal circulation, host-range promiscuity, and immune evasion, with reduced antiviral binding in a fatal human isolate.

[See details](#)

2026-05-27

Genotype Diversity of Highly Pathogenic Avian Influenza H5N1 Clade 2.3.4.4b in Pennsylvania Poultry During Disease Outbreak from April 2022 to March 2023.

Journal: Viruses

Authors: Deepanker Tewari, Manoj K Sekhwal, Chrislyn Nicholson, Mary L Killian, Corey Zellers, Julia Livengood, Kristina Lantz, Mia Torchetti, Alex Hamberg

Eight H5N1 clade 2.3.4.4b genotypes identified in 2022 Pennsylvania outbreak, with B3.3 predominant in backyard flocks. Outbreak driven by wild bird migration, with A1 as earliest detected. B3.3 no longer in circulation by September 2023.

[See details](#)

2026-04-28

Emergence and Rapid Spread of a New Reassortant High Pathogenicity H5N1 Clade 2.3.4.4b Avian Influenza Virus in Nigeria.

Journal: Influenza Other Respir Viruses

Authors: Clement Meseko, Bianca Zecchin, Emilie Wolali Go-Maró, Marta Dianati, Nicodemus Mkpuma, Bitrus Inuwa, Judith Bakam, Kayode Olawuyi, Dorcas Gado, Edoardo Giussani, Alice Fusaro, Alessio Bortolami, Elisa Palumbo, Calogero Terregino, Isabella Monne

A new reassortant H5N1 clade 2.3.4.4b avian influenza virus, EA-2024-DV, has emerged and rapidly spread in Nigeria and West Africa, replacing the previously dominant EA-2020-C genotype. This highlights the region's vulnerability to novel introductions and the need for sustained surveillance.

[See details](#)

2026-05-12

Influenza Vaccine Effectiveness in School Outbreaks During a A(H3N2) Subclade K (J.2.4.1)-Dominated Season in Beijing, China, 2025-26.

Journal: Int J Infect Dis

Authors: Ying Shen, Chunna Ma, Daitao Zhang, Weixian Shi, Wei Duan, Jia Li, Lu Zhang, Dan Wu, Jiaojiao Zhang, Jiaxin Ma, Yingying Wang, Xiaodi Hu, Shuning Yan, Yuanzhi Di, Jiachen Zhao, Hui Xu, Guilan Lu, Yimeng Liu, Quanyi Wang, Peng Yang, Zhaomin Feng

This study found that influenza vaccination offered 30.0% protection against symptomatic A(H3N2) infection in school outbreaks during the 2025-26 season in Beijing, emphasizing its value and the need for continuous vaccine optimization and surveillance.

[See details](#)

2026-05-09

Development of a nano-emulsion and evaluation of its intradermal adjuvant function of Swine Influenza H3N2 Vaccine.

Journal: Virol J

Authors: Zhuoyu Ruan, Bihua Deng, Wenzhu Yin, Fang Ma, Yu Lu, Haiyan Wang

VP nano-emulsion adjuvant, composed of squalene, sea buckthorn oil, and Poly(I: C), enhanced intradermal swine influenza H3N2 vaccination in mice, inducing robust, durable, Th1-biased immunity, superior to intramuscular administration, with minimal local reactogenicity.

[See details](#)

2026-05-11

H5N1 avian influenza in dairy cattle: Molecular adaptation, transmission mechanisms, and control strategies.

Journal: Virology

Authors: Kaidi Ding, Yi Ding

H5N1 avian influenza has spread to dairy cattle in the US, causing mastitis and economic losses, with potential public health risks. This review (2024-2026) examines mammalian adaptation, transmission (mouth-to-teat, contaminated milk), and control strategies, emphasizing "One Health" approach.

[See details](#)

2026-05-27

Reassortant High Pathogenicity Avian Influenza A(H5N1) Viruses During the Reemergence in Uruguay Suggest Increasing Genetic Diversity in South America.

Journal: Viruses

Authors: Ana Marandino, Gonzalo Tomás, Yanina Panzera, Valeria Uriarte, Virginia Russi, Ramiro Pérez, Lucía Bassetti, Raúl Negro, Sirley Rodríguez, Ruben Pérez

Reassortant H5N1 viruses in Uruguay (2026) show Eurasian HA, NA, MP, and American internal genes, with PB2 variation. Neuraminidase changes reduced RT-qPCR sensitivity, indicating diagnostic challenges and increasing genetic diversity in South America.

[See details](#)

2026-05-25

Central Nervous System Involvement by Novel Clade 2.3.2.1e H5N1 Avian Influenza Virus in a Pediatric Patient.

Journal: Open Forum Infect Dis

Authors: Phung Nguyen The Nguyen, Nguyen Thanh Hung, Ngo Ngoc Quang Minh, Nguyen Thi Thu Hong, Nguyen Thi Thanh Huong, Cao Minh Hiep, Le Nguyen Thanh Nhan, Tran Van Dinh, Du Tuan Quy, Tran Thanh Thuc, Tran Minh Nhut, Nguyen Thi Han Ny, Lam Anh Nguyet, Le Nguyen Truc Nhu, Do Duong Kim Han, Truong Hoang Chau Truc, Le Thi Tam Uyen, Nghiem My Ngoc, Tran Nguyen Phuong Thao, Tran Thi Thanh Tam, Sandy Tze-Minn Mak, Jurre Y Siegers, Sebastian Maurer-Stroh, Nguyen Thanh Dung, Erik A Karlsson, Guy Thwaites, Chee Wah Tan, Nguyen Van Vinh Chau, Le Van Tan, SEACOVARIANTS and H5N1 Consortia

Novel clade 2.3.2.1e H5N1 detected in CSF of an 8-year-old with meningoencephalitis, no respiratory symptoms. Higher HA antibodies in CSF than serum. Clinicians should consider H5N1 in neurological presentations.

[See details](#)

2026-05-16

Highly pathogenic avian influenza A(H5N1) in poultry and domestic cats and occupational exposure among veterinary and other first responders, Germany, February 2026.

Journal: Euro Surveill

Authors: Aparna Dressler, Christiane Wagner-Wiening, Bettina Tegtmeyer, Susanne Haag-Milz, Bettina Demattio, Ralf Dürrwald, Timm Harder, Andreas Salditt, Judith Köster

In February 2026, an HPAI A(H5N1) outbreak in German poultry infected cats and exposed 17 humans, with one showing symptoms but testing negative for H5N1. This underscores zoonotic risks, mammalian spillover, and the need for coordinated One Health responses.

[See details](#)

2026-04-17

Neuraminidase-inhibiting antibodies boosted by H1N1pdm infection cross-react differently with H5N1 of clades 2.3.4.4b and 2.3.2.1a.

Journal: Emerg Microbes Infect

Authors: Kong Yen Liew, Dinah Binte Aziz, Yee Teng Chan, Chee Wah Tan, Paul Tambyah, Yee-Joo Tan

Recent H1N1pdm infection elicited strong NA-inhibiting (NAI) antibody responses against older H1N1pdm and cross-reactive NAI against clade 2.3.4.4b H5N1, but not clade 2.3.2.1a, due to antigenic divergence. Cross-reactive NAI responses waned by day 90 post-infection, highlighting their limited durability.

[See details](#)

Relevant news

This section presents official reports from health agencies, manufacturers and press releases with reliable sources.

2026-05-05

Sampling reveals possible novel sources of H5N1 avian flu transmission on dairy farms

Source: CIDRAP

The study found H5N1 avian flu virus in air, wastewater, and milk on California dairy farms, with potential transmission via aerosols and environmental contamination, posing risks to cows, wildlife, and humans.

[See details](#)

2026-04-29

WHO reports H5N1 death among variant zoonotic flu cases seen this year

Source: CIDRAP

In Q1 2026, WHO reported 13 avian/swine flu cases, including a fatal H5N1 case in a Bangladeshi child with poultry exposure. Cases included H5N1 (4), H9N2 (5), and H1/H3 variants (4), mostly in children. Risk to general population remains low, with no sustained human-to-human transmission.

[See details](#)

2026-04-23

More California marine mammals confirmed to have H5N1 avian flu, as USDA tracks poultry outbreaks in Midwest

Source: CIDRAP

In California, 58 marine mammals (57 sea lions, 1 otter) tested positive for H5N1 avian flu, with most cases in San Mateo County. Symptoms included respiratory issues, tremors, and neurologic signs. Additionally, four new poultry outbreaks were reported in the Midwest, affecting 62,900 birds. Wild bird detections, including Bald Eagles and gulls, have also been noted.

[See details](#)

2026-04-16

Avian flu detected in Idaho dairy cows as study explores role of virus RNA detection in bovine semen

Source: CIDRAP

H5N1 avian flu detected in Idaho dairy cows, with RNA found in bull semen, though live virus not identified. Study inconclusive on semen as a virus conduit. APHIS reports recent outbreaks in commercial poultry operations, affecting 1.6 million birds in 30 days.

[See details](#)

2026-04-30

Avian flu detections drop across the US

Source: CIDRAP

Avian flu detections in US poultry and wild birds have declined, with one new poultry case in South Dakota affecting 60 birds. Over 30 days, 15 commercial and 8 backyard flocks were affected, totaling 660,000 birds. February saw the highest poultry impact, with 11.41 mill

[See details](#)

2026-05-29

Global Human Cases with Avian Influenza A(H5N1), 1997-2026

Source: CDC

First human cases in Hong Kong 1997: 18 confirmed, 6 deaths. Since 1997: >1,000 cumulative sporadic cases across 25 countries including the US; ~48% case fatality rate. Transmission via direct contact with infected poultry; no sustained human-to-human spread. Current clade 2.3.4.4b strains circulating since fall 2021 are genetically distinct from earlier H5N1 lineages.

[See details](#)

Clinical Studies

This section presents relevant clinical trials.

2025-11-16

Immunogenicity and Safety of 2 Doses of Avian Influenza A (H5N1) Vaccine Administered 3 vs. 8 Weeks Apart

Status: Active not recruiting

Sponsor(s): Canadian Immunization Research Network, Dalhousie University, IWK Health Centre, Public Health Agency of Canada (PHAC), Canadian Center for Vaccinology, CHU de Quebec-Universite Laval, Vaccine Evaluation Center, Canada, McGill University Health Centre/ Research Institute of the McGill University Health Centre

This study compares the immunogenicity and safety of two dosing intervals (3 vs. 8 weeks) of the Arepanrix™ H5N1 vaccine, approved for use in high-risk individuals due to recent H5N1 circulation in North America. Limited data exists on the impact of dosing intervals on vaccine response and tolerability.

[See details](#)

2024-06-21

Single Dose Texas 2017 (H3N2) Challenge Study

Status: Completed

Sponsor(s): Duke University, United States Department of Defense, Owlstone Ltd, Darwin Biosciences

This study uses a controlled human infection model with H3N2 (A/Texas/71/2017) to identify early infection markers in exhaled breath and saliva, recruiting 40 healthy volunteers.

[See details](#)

2025-11-27

Establishing a Controlled Human Infection Model for Influenza H3N2 as a Foundation for Pandemic Preparedness

Status: Not yet recruiting

Sponsor(s): Dalhousie University, Canadian Center for Vaccinology, McGill University Health Centre/Research Institute of the McGill University Health Centre

The overall objective is to establish an influenza Controlled Human Infection Model (CHIM) in Canada that can be used to assess the safety and efficacy of candidate vaccines, biologics, and therapeutics targeting influenza viruses.

[See details](#)

2024-09-25

GEneRating Mucosal Immunity After INfluenzA Infection and Vaccination in Lung and Lymphoid Tissue

Status: Recruiting

Sponsor(s): Imperial College London, Imperial College Healthcare NHS Trust

This experimental medicine study aims to compare immune responses in healthy adult volunteers aged 18-55 years against influenza vaccination and infection in the upper and lower respiratory tract, following administration of a live-attenuated influenza vaccine delivered by nasal spray versus influenza A (H3N2) viral challenge.

[See details](#)

2025-06-16

Pilot Influenza Challenge Study

Status: Active not recruiting

Sponsor(s): Daniel Hoft, MD, PhD

This pilot study examines H3N2 influenza infection dynamics and immune responses in healthy participants, assessing pre-existing antibodies' protective role, symptom onset, and immune response timing through blood samples, NP swabs, and exhaled virus collection during inp

[See details](#)

2026-03-25

Phase 2a Study of the Efficacy and Safety of TRX-100 in a Human Influenza A Challenge Model

Status: Not yet recruiting

Sponsor(s): Traws Pharma, Inc.

This will be a randomized, double-blind, placebo-controlled proof of concept study to evaluate the prophylactic efficacy and safety of orally administered TRX-100 in healthy adults challenged with influenza A/France/759/2021 (H1N1) virus.

[See details](#)

2024-04-16

A Study to Find and Confirm the Dose and Assess Safety, Reactogenicity and Immune Response of a Vaccine Against Pandemic H5N1 Influenza Virus in Healthy Younger and Older Adults

Status: Completed

Sponsor(s): GlaxoSmithKline (Belgium)

The aim of this study is to evaluate the safety, reactogenicity and immunogenicity of the Flu Pandemic messenger RNA (mRNA) vaccine (including dose-finding and dose-confirmation) administered in healthy adults 18 to 85 years of age.

[See details](#)

Guidelines and practical information

This section lists official manuals of recommendations for clinical practice or public health policy published by leading health organizations.

January 2024	Interim Guidance for Employers to Reduce Exposure to Avian Influenza A Viruses for People Working with Animals
August 2024	Practical interim guidance to reduce the risk of infection in people exposed to avian influenza viruses
June 2024	Highly Pathogenic Avian Influenza A(H5N1) Virus in Animals: Interim Recommendations for Prevention, Monitoring, and Public Health Investigations (CDC)
June 2024	Prevention and Antiviral Treatment of Avian Influenza A Viruses in People (CDC)
May 2024	Avis du COVARS du 24 mai 2024 - Point sur la situation liée au virus influenza H5N1 (MESRI)
December 2023	Considerations for emergency vaccination of wild birds against high pathogenicity avian influenza in specific situations (WOAH)
June 2023	Enhanced surveillance of severe avian influenza virus infections in hospital settings in the EU/EEA (ECDC)
January 2022	Guidelines for the clinical management of severe illness from influenza virus infections (WHO)
December 2021	Avis relatif à la prévention de la transmission à l'homme des virus influenza porcins et aviaires (HCSP)

Fact sheets

Transmission

Influenza A viruses are segmented, negative-sense single-stranded RNA viruses, members of the Orthomyxoviridae family. The antigenic diversity of these viruses arises from two surface glycoproteins: hemagglutinin (HA) and neuraminidase (NA). Combinations of these proteins create numerous influenza subtypes, with currently 18 HA and 11 NA subtypes recognized in the environment. Although avian influenza viruses spread mainly among waterfowl, particularly Anseriformes and Charadriiformes, as well as in other susceptible bird species such as Galliformes. Unlike most other avian influenza viruses, A(H5N1) 2.3.4.4b has infected more than 200 mammal species and they can occasionally infect humans but no sustained human-to-human transmission has been identified.

Diagnosis

Appropriate samples for influenza tests should be rapidly taken and processed from patients with a relevant exposure history within ten days preceding symptom onset. A(H5N1) viruses have been detected in raw milk from infected dairy cows in some locations.

Symptoms

The incubation period for A(H5N1) infection is typically two to five days after the last known exposure. A(H5N1) influenza virus infection can cause a range of diseases in humans, from mild to severe, and in some cases, it can even be fatal. Symptoms are primarily respiratory, including fever, malaise, cough, sore throat, and muscle aches. Other early symptoms may include conjunctivitis and other non-respiratory symptoms. The infection can quickly progress to severe respiratory illness and neurological changes. A(H5N1) virus has also been detected in asymptomatic individuals.

Treatment

Influenza patients should be managed properly to prevent severe illness and death. Patients with laboratory-confirmed should be treated with antiviral medicines like oseltamivir as soon as possible.

Vaccination

Vaccine development leading to the licensure of three H5N1 vaccines - clade 1 and 2.1 - by the FDA and EMA under the trade name Audenz® / Aflunox®, Preprandix® / Pumarix®, and Foclivia® / Adjupanrix®.