# 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.

EDITION **Mar. 2026** No. **17**

**Editors**: Yoann Allier, Douae Ammour, Mathilde Certoux, Dahlia Chebbah, Vincent Cicculi, Nathan Claveau, Mario Delgado-Ortega, Sandrine Halfen, Charly Kengne, Rana Lebdy, Diana Molino, Mélanie Nguyen Marzine, Eric Rosenthal, Amandine Verga Gerard, Armelle Pasquet, et Eric D'Ortenzio, avec la participation de Marie Winter (OPEN-ReMIE)

ANRS Emerging Infectious Diseases - Paris, France

## Situation at a glance

- 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 was identified.
- On 29 March 2026, Cambodia reported its third human case of A(H5N1) for the year.
- 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.

# Scientific articles

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

2026-03-27

## Impact of maternal antibodies and weaning stress on the replication and transmission of human H3N2 influenza A in piglets.

**Journal**: J Virol

**Authors**: Giovana Ciacci Zanella, Matias I Cardenas, Carl R Hutter, Celeste A Snyder, Meghan Wymore Brand, Bailey Arruda, Daniel R Perez, Tavis K Anderson, Daniela S Rajão, Amy L Baker

Matched MDA reduced nasal shedding and transmission of human-like H3N2 in piglets, while mismatched MDA did not. Weaning stress increased shedding and transmission in pigs with mismatched MDA, highlighting critical control points in swine production to mitigate interspecies and swine-to-swine transmission.

**See details**

2026-03-28

## Drug Repurposing of Verapamil for H1N1 Influenza Virus Infection: A Multi-Target Strategy Revealed by Network Pharmacology and Experimental Validation.

**Journal**: Int J Mol Sci

**Authors**: Yan Cao, Jiajing Wu, Xuena Li, Feifan Qiu, Shuo Wang, Bingshuo Qian, Lingjun Fan, Yueqi Wang, Kun Xue, Junkui Zhang, Beilei Shen, Yuwei Gao

Verapamil, an L-type calcium channel blocker, demonstrates antiviral activity against H1N1-UI182, improving survival, reducing viral load, and mitigating inflammation via NF-κB. Optimal efficacy with pre-treatment suggests early-stage intervention. Network pharmacology pr

**See details**

2026-03-22

## Prophylactic and therapeutic efficacy of monoclonal antibodies against H5N1 influenza virus.

**Journal**: Int J Antimicrob Agents

**Authors**: Antonios-Periklis Panagiotopoulos, Cleo Anastassopoulou, Kyriaki Ranellou, Ilias Mariolis, Athanasios Tsakris

mAbs targeting conserved H5N1 epitopes, neuraminidase, M2, and nucleoprotein show broad neutralizing and protective efficacy in animal models. Clinical trials demonstrated safety and no resistance, despite discontinued development. Integrating these mAbs into pandemic pre

**See details**

2026-03-20

## Intranasal prime-boost immunization with trivalent influenza virus neuraminidase proteins and conserved HCA2 sequences fused to a circularly permuted E. coli heat-labile enterotoxin B subunit.

**Journal**: Vaccine

**Authors**: Hao-Chan Hung, Kai-Wun Jheng, Huan-Yu Cheng, He-Chin Hsieh, Chung-Chu Chen, Shih-Che Sue, Wen-Chun Liu, Suh-Chin Wu

Intranasal trivalent NA vaccine with LTB(TT)-HCA2 adjuvant induced high IgG, NAI, and replication-inhibition antibodies, protecting mice against H1N1 and H3N2. Four-dose regimens enhanced responses but did not confer H7N9 cross-immunity.

**See details**

2026-04-13

## The temporal sequence of influenza H1N1 and Mycoplasma pneumoniae co-infection causes disease severity in Syrian hamster models.

**Journal**: Front Microbiol

**Authors**: Junchi Ma, Yanyan Li, Weihua Jin, Xueqian Xie, Aiyi Li, Yanan Wu, Fengmei Yang, Suqin Duan, Mingxue Li, Haiting Long, Zhanlong He, Yuan Zhao

Syrian hamsters co-infected with H1N1 followed by Mp (F-M group) showed severe histopathological lesions, higher pathogen loads, and dysregulated cytokine responses, emphasizing the impact of infection order on disease severity.

**See details**

2026-03-21

## Comparative evaluation of cell lines and their serum-free adapted derivatives for H1N1 influenza A virus propagation: bridging laboratory research and industrial vaccine production application.

**Journal**: Vaccine

**Authors**: S Furkan Demirden, Ilgin Kimiz-Gebologlu, Suphi S Oncel

This study evaluates human cell lines and their serum-free adapted derivatives for H1N1 influenza A virus propagation, aiming to identify optimal platforms for vaccine production.

**See details**

2026-03-28

## Systems-Level Analysis of HPAI H5N1 Infection in Ducks: Integrating Transcriptomic, Proteomic, and Phosphoproteomic Data.

**Journal**: Int J Mol Sci

**Authors**: Periyasamy Vijayakumar, Anamika Mishra, Kandasamy Rajamanickam, Ashwin Ashok Raut

This study employs a multi-omics approach to elucidate HPAI H5N1 pathogenesis in ducks, identifying key signaling pathways (RIG-I-like, TLR, NOD-like, NF-κB, JAK/STAT) and hub genes (e.g., STAT1, DDX58, MYD88) in duck lung tissue. Phosphoproteomic data corroborates these findings, suggesting potential therapeutic targets for avian influenza.

**See details**

2026-03-18

## Correction to "An Overview of the H5N1 mRNA Vaccine Pipeline".

**Journal**: Influenza Other Respir Viruses

**Authors**:

**See details**

2026-03-28

## Immunogenicity and safety of MF59-adjuvanted H5N1 pandemic influenza vaccine in healthy infants and children: a phase 2 randomized, observer-blind, multicenter study.

**Journal**: Vaccine

**Authors**: Airi Põder, Mitzi Trinidad-Aseron, Esther Van Twuijver, Eve Versage, Matthew Hohenboken

This phase 2 study evaluated six MF59-adjuvanted H5N1 vaccine formulations in children aged 6 months to <9 years. All formulations induced robust immune responses, with higher adjuvant content enhancing magnitude and persistence. Safety profiles were similar across groups

**See details**

2026-03-12

## Influenza Vaccine Effectiveness Against Influenza A(H1N1)pdm09-Associated Hospitalizations With SARI in Beijing, China, in the 2024-2025 Season.

**Journal**: Influenza Other Respir Viruses

**Authors**: Chunna Ma, Ying Sun, Jiaxin Ma, Yingying Wang, Xiaodi Hu, Ying Shen, Li Zhang, Jiaojiao Zhang, Lu Zhang, Wei Duan, Jia Li, Quanyi Wang, Daitao Zhang, Peng Yang

2024-2025 influenza vaccine showed 18.8% effectiveness against A(H1N1)pdm09-associated SARI hospitalizations in Beijing, with higher VE in children (45.4%) and adults (43.8%), but limited effectiveness in older adults (8.6%). Among those with chronic conditions, VE was 18

**See details**

2026-03-23

## Nasal RNA-scaffold-protein vaccine protects mice from human H5N1 clade 2.3.4.4b virus lethal infection and safeguards against vaccine-unmatched viruses.

**Journal**: EBioMedicine

**Authors**: Joy-Yan Lam, Chun-Kit Yuen, Shuk-Kwan Cheung, Pak-Him Cheung, Kwok-Yung Yuen, Kin-Hang Kok

RSPVac nasal vaccine induces strong mucosal immunity, protecting mice from lethal H5N1 clade 2.3.4.4b infection and offering cross-protection against unmatched viruses. It elicits robust antibody and T-cell responses, transient cytokine expression, and controlled neutrophil activation. Mutant RSPVac shows impaired efficacy, suggesting a complex activation mechanism.

**See details**

2026-03-13

## Population immunity, post-vaccine and post-infection antibody responses to influenza A (H3N2) subclade J.2 and K (J.2.4.1) viruses, Hong Kong, 2025.

**Journal**: Euro Surveill

**Authors**: Samuel Ms Cheng, Nancy Hl Leung, Eunice Y Shiu, Ricky Wk Wong, Niki Ym Au, Xiaotong Huang, Natalie Km Kwok, Coco Hc Chan, John Kc Li, Leo Ch Tsang, Tsz Chun Kwan, Tim K Tsang, Leo Lm Poon, Benjamin J Cowling, Malik Peiris

This study evaluated antibody responses to 2025 H3N2 subclades J.2 and K in Hong Kong. Human sera showed cross-reactivity between subclades, unlike ferret sera. Vaccination with J.2 vaccines increased antibody titres against subclade K, with recombinant haemagglutinin vaccines being more effective than egg-based ones.

**See details**

2026-03-13

## Infection of ratites with clade 2.3.4.4b HPAIV H5N1: Potential implications for zoonotic risk.

**Journal**: Emerg Microbes Infect

**Authors**: Holly A Coombes, Jacob Terrey, Audra-Lynne Schlachter, Phoebe McCarter, Isabella Regina, Richard Hepple, Natalie McGinn, James Seekings, Jayne Cooper, Benjamin Clifton, Benjamin C Mollett, Marco Falchieri, Alejandro Nunez, Scott M Reid, Joe James, Ashley C Banyard

We detected H5N1 high pathogenicity avian influenza in captive Greater Rhea (Rhea americana). Viral genetic analysis revealed the mammalian associated PB2-E627 K mutation, indicating selection of mammalian-relevant mutations in ratites. Pathologic investigation of available tissues demonstrated severe multifocal necrotising inflammation, and a strong vasculotropism.

**See details**

2026-03-13

## Receptor-binding specificity and antigenic properties of a genotype D1.1 A(H5N1) influenza virus isolated from a human.

**Journal**: Emerg Microbes Infect

**Authors**: Ahmed Kandeil, Pradeep Chopra, Sean D Ray, Balasaheb K Ghotekar, Charlene Ranadheera, Trushar Jeevan, Thomas Fabrizio, Adam Rubrum, Geert-Jan Boons, Stephen Mark Tompkins, Nathalie Bastien, Richard J Webby

Genotype D1.1 A(H5N1) from British Columbia binds avian receptors, showing no human adaptation. Antigenically, it is covered by current vaccine candidates.

**See details**

2026-03-27

## Genomic Epidemiology of Influenza A(H3N2) in Pakistan: 2025-2026 Season Analysis.

**Journal**: J Med Virol

**Authors**: Nazish Badar, Muhammad Salman, Abdul Ahad, Hamza Ahmed Mirza

See details

2026-04-07

## MF59-adjuvanted A/Astrakhan influenza vaccine induces cross-neutralizing H5N1 antibodies in ferrets against circulating clade 2.3.4.4b viruses.

**Journal**: NPJ Vaccines

**Authors**: Karen Segovia, Raveen Rathnasinghe, Christopher Patton, Byungjoon Kwon, Ray A Longstaff, Dirk Hofmann, Kulwinder K Banger, Howard Xu, Marc Lacey, Ethan Settembre, Giuseppe Palladino, Alexander T Kennedy, Nedzad Music

The study evaluated the MF59-adjuvanted A/Astrakhan H5N8 influenza vaccine in ferrets, demonstrating robust neutralizing titers against clade 2.3.4.4b H5N1 viruses, with cross-reactivity reduced against strains with the A156T HA mutation. A second dose boosted titers, highlighting the vaccine's potential for pandemic preparedness.

See details

# Relevant news

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

2026-03-17

### More animals die from H5N1 avian flu at Ano Nuevo State Park in California

**Source**: CIDRAP

H5N1 avian flu outbreak at Ano Nuevo State Park, California, confirmed in 11 marine mammals, with likely more cases. First detection in California marine mammals, causing respiratory and neurologic symptoms. Park closed sea-viewing areas, but 80% of adult female seals had

See details

2026-03-31

### Quick takes: CDC warning on raw cheese, H5N1 avian flu case in Cambodia, HIV drug access

**Source**: CIDRAP

CDC warns against Raw Farm-brand raw cheddar cheese linked to E. coli outbreak. Cambodia reports third H5N1 avian flu case in 2026, linked to poultry. MSF criticizes Gilead for restricting access to HIV preventative lenacapavir.

See details

2026-04-02

## Quick takes: Moringa Salmonella probe over, H7 flu case in Taiwan, H5N1 outbreaks in US poultry

**Source**: CIDRAP

CDC concluded investigations into drug-resistant Salmonella outbreaks linked to moringa products, with 10 cases and 3 hospitalizations. Taiwan reported its first locally transmitted H7 avian flu case in a poultry worker. USDA reported multiple H5N1 outbreaks in poultry, affecting over 5.2 million birds.

**See details**

2026-03-26

## Avian flu strikes 9 more Indiana poultry facilities

**Source**: CIDRAP

USDA reports 9 new H5N1 outbreaks in Indiana poultry, affecting 20,000+ birds, with additional cases in Utah and West Virginia. Nationwide, 85 flocks (45 commercial, 40 backyard) affected, totaling 10.10 million birds. Indiana has 26 commercial and 11 backyard outbreaks.

**See details**

2026-04-09

## Indiana tracks more avian flu in hard-hit counties

**Source**: CIDRAP

Indiana reports new H5N1 outbreaks in Elkhart and LaGrange counties, affecting 111,300 birds. Nationwide, 56 flocks, 4.97M birds impacted in 30 days. February saw peak activity with 11.41M poultry affected. California's Año Nuevo State Park, closed due to H5N1 in marine mammals, is set to reopen.

**See details**

2026-03-24

## Indiana: More than 350,000 birds killed in massive avian flu outbreak

**Source**: CIDRAP

Indiana's avian flu outbreak has killed 350,000+ birds this month, with 10M+ since 2022, affecting poultry in LaGrange/Elkhart counties. Biosecurity is critical to prevent spread. While cattle remain uninfected, experts warn of potential livestock transmission. Despite fa

**See details**

# Clinical Studies

This section presents relevant clinical trials.

2024-09-23

## Dose, Safety, and Pathogenicity of a New Influenza A H3N2 Challenge Strain

**Status**: Completed

**Sponsor(s)**: hVIVO (United Kingdom)

This study aims to determine the optimal dose, safety, and pathogenicity of a new Influenza A H3N2 challenge strain in healthy adults aged 18-55. Part A will randomly allocate 40 participants to receive one of two virus doses. Part B will use the findings from Part A to administer the most appropriate dose(s) to further participants.

**See details**

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 evaluates the immunogenicity and safety of the H5N1 vaccine (Arepanrix™) administered in two doses, comparing 3-week and 8-week intervals. Limited data exist on the impact of dosing intervals, and this research aims to address that gap, particularly relevant given recent H5N1 circulation in North America.

**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 breath and saliva. 40 healthy volunteers (18-45) will receive either placebo or virus, with responses measured through clinical, lab, immunological, digit

**See details**

2025-02-23

## H5N1 Milk Detection Study

**Status**: Recruiting

**Sponsor(s)**: Emory University, National Institute of Allergy and Infectious Diseases (NIAID)

This study investigates if consuming pasteurized milk containing inactive H5N1 virus particles can lead to detectable viral presence in the nose or throat, and if it elicits an antibody response. Findings aim to inform CDC's understanding of milk consumption's impact on flu surveillance.

**See details**

2025-04-27

## Human Infection Study of H3N2 Influenza in Healthy Adults

**Status**: Active not recruiting

**Sponsor(s)**: University of Melbourne, National Institute of Allergy and Infectious Diseases (NIAID), WHO Collaborating Centre for Reference and Research on Influenza

This study investigates immune responses to H3N2 influenza in healthy adults (18-50) during and post-infection in a controlled inpatient setting, using a clinically-researched H3N2 challenge virus, anticipating mild to moderate symptoms. It marks Australia's first flu challenge study.

**See details**

2025-10-10

## BPL-1357 Against H1N1 Influenza Virus Challenge

**Status**: Recruiting

**Sponsor(s)**: National Institute of Allergy and Infectious Diseases

This study evaluates the efficacy of an experimental flu vaccine, BPL-1357, against H1N1. It involves two phases: Phase A, with outpatient vaccinations and monitoring, and Phase B, with controlled H1N1 exposure in a hospital setting. Participants receive either nasal or injectable vaccine, or placebo, and are monitored for immune response and symptoms.

**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**

2026-03-31

## Study of Different Formulations of Vaccines Encoding the RSV Monovalent Antigen or the Flu H5 Antigen in Participants 18 to 49 Years of Age

**Status**: Not yet recruiting

**Sponsor(s)**: Sanofi (Canada)

This study evaluates the safety and immunogenicity of various vaccine formulations encoding RSV monovalent antigen or Flu H5 antigen in healthy adults aged 18-49. Participants are divided into six arms, with Stage 1 durations of 6-7 months and Stage 2 durations of 7 months.

**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 investigates influenza infection dynamics and immune responses in healthy participants challenged with H3N2. It examines pre-existing antibodies' protective role, tracks symptoms, and collects blood, NP swabs, and exhaled virus samples. Participants are monitored for up to 10 days, with follow-ups post-discharge.

**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 (Group)

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® / Afllunox ®, Preprandix® / Pumarix®, and Foclivia® / Adjupanrix®.