



NIAID Research Key to H5N1 Influenza Preparedness Efforts

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Since 1996, H5N1 influenza viruses have circulated in at least 23 countries, primarily affecting wild birds and poultry and sporadically infecting people in close contact with infected birds. In recent years, a strain of highly pathogenic H5N1 avian influenza virus (HPAI H5N1) has spread to infect more than 50 mammalian species.

This spring, an HPAI H5N1 outbreak was detected among dairy cows and has now spread to cattle in 16 states leading to infections among dairy and poultry workers. Although the virus so far has not demonstrated genetic mutations enabling person-to-person spread, NIAID scientists and NIAID-funded researchers have been working to closely monitor the outbreak, understand spread among animals, and develop potential prevention and treatment methods as part of larger U.S. government pandemic preparedness efforts.

The Work of the CEIRRs

The NIAID-funded [Centers of Excellence for Influenza Research and Response](#), or CEIRRs, have played a major role in the Institute's overall influenza research program and in responding to the ongoing HPAI H5N1 outbreak among U.S. dairy cows. The six U.S.-based CEIRRs study influenza's natural history, transmission and pathogenesis (how the viruses cause disease) and have long monitored wild birds to detect HPAI H5N1 and other influenza viruses.

Since the U.S. dairy cattle outbreak was detected in March 2024, the CEIRRs have: tested retail milk for evidence of HPAI H5N1; conducted tests to determine at what [temperatures the virus is inactivated in milk](#); performed animal tests to determine the potential risk of HPAI H5N1 infection when [consuming raw milk and raw milk-based products](#); completed studies designed to determine how long HPAI H5N1 viruses remain viable on surfaces, such as metal and rubber; conducted animal studies to determine how efficiently HPAI H5N1 viruses [transmit among mice and ferrets](#); performed [genetic mutation studies](#) to understand the potential risk for human-to-human transmission; and conducted research to understand how previous exposure to other influenza viruses impact potential disease severity from HPAI H5N1.

“The CEIRRs have been instrumental in responding to the U.S. outbreak of HPAI H5N1,” said NIAID Director Jeanne M. Marrazzo, MD, MPH. “Their work and similar efforts by NIAID scientists at Rocky Mountain Laboratories (RML) in Montana inform our real-time understanding of the evolution of the viruses and what we must do as public health professionals to best prepare should HPAI H5N1 present a larger threat to humans.”

Finding New Treatments

Currently, the primary treatment for HPAI H5N1 influenza infection is oseltamivir (Tamiflu), which, ideally, should be taken within 48 hours of symptom onset. To bolster the pool of available treatments, the CEIRRs, other NIAID-funded researchers and scientists at NIAID’s Vaccine Research Center (VRC) and RML also have been working to find potential therapeutics. This effort involves early-stage testing of numerous broad-spectrum antiviral drugs, exploring the use of host-acting medicines, examining the repurposing of existing antivirals, testing anti-inflammatory compounds, and identifying, characterizing, and performing scaled-up manufacturing of monoclonal antibodies for treatment and prevention studies.

One of the outgrowths of this work is a first-in-human clinical study of a new antiviral agent targeting the genetic material tied to the influenza viral protein, or nucleoprotein, that is expected to begin in early 2025.

Vaccine Development

The U.S. stockpile currently contains vaccines to prevent severe disease from HPAI H5N1 infection. Because the U.S. Centers for Disease Control and Prevention has determined that the current risk of HPAI H5N1 to the public is low, these vaccines have not been deployed. The U.S. Department of Health and Human Services’ Biomedical Advanced Research and Development Authority (BARDA) is responsible for updating these vaccines, if necessary, to address new strains of HPAI H5N1 and formulate new antigens, the active parts of vaccines designed to stimulate an immune response. NIAID is responsible for developing new vaccine candidates and conducting targeted studies of existing vaccines.

Development of H5N1 influenza vaccines has been a NIAID priority for many years before the current outbreak. NIAID is currently funding: a [new H5N1 avian flu vaccine](#) candidate that can potentially spur immunity to various strains of the virus and offer long-lasting protection. That vaccine is set to begin early-stage human clinical trials in 2025. NIAID-supported investigators are also developing vaccine adjuvants that are being evaluated as components of candidate mRNA and inactivated H5N1 influenza vaccines. Adjuvants are substances that are added to some vaccines to enhance the immune response and improve the vaccine effectiveness.

Additionally, efforts toward the development of a universal influenza vaccine—one, that in theory, could neutralize most or all influenza virus strains and eliminate the need for an annual flu vaccination—has long been a NIAID goal. A [universal influenza vaccine candidate](#) called H1ssF developed by NIAID VRC scientists performed well in an early-stage clinical trial and is currently undergoing further evaluation, including testing it against HPAI H5N1 in preclinical studies.

Another [universal influenza vaccine candidate, called BPL-1357](#), developed by scientists in NIAID's Division of Intramural Research, performed well in early-stage clinical studies and is expected to be evaluated for protective efficacy in Phase 2 human clinical studies in early 2025. This vaccine candidate is also being evaluated against HPAI H5N1 and has demonstrated excellent protection in preclinical studies.

Answering Important Scientific Questions

All of these HPAI H5N1 activities align with NIAID's overarching [H5N1 influenza research agenda](#) issued in May 2024. The plan focuses on increasing understanding of the biology of H5N1 viruses and the factors that influence their ability to transmit and cause disease; developing and evaluating prevention strategies, such as vaccines; advancing existing and novel treatments, including antivirals and monoclonal antibodies; and supporting strategies for detecting H5N1 virus.

"NIAID's influenza research will be an enduring priority as influenza viruses are constantly evolving," Dr. Marrazzo said. "Our H5N1 work complements ongoing influenza research and focuses on answering important scientific questions relevant to the current outbreak in keeping with our vital role in pandemic preparedness."

Many questions related to the current HPAI H5N1 situation remain to be answered. Among them: the source of the initial outbreak among U.S. dairy cows; how the virus is spreading between farms; the risk to people from infected dairy cows or migratory bird strains of H5N1 why most human HPAI H5N1 cases so far in the U.S. have resulted in mild disease; and what level of protection to H5N1 people may have due to prior exposure to other influenza strains.

"We may never know the answers to all of these questions, but as a scientific institute, we absolutely must do our best to understand the virus and how it may evolve, so that we can optimally protect the American public with new countermeasures," Dr. Marrazzo said.

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