



# Respiratory Viral Infections: Highlights from IDWeek 2024

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IDWEEK 2024, held in Los Angeles, California, October 16<sup>th</sup>–19<sup>th</sup>, was an opportunity for the >12,000 attendees to hear about state-of-the-art scientific updates in infectious diseases. Respiratory viral infections were prominently featured, with myriad presentations on the epidemiology, prevention, and management of several important and emerging pathogens. Highlights of the program are listed below.

## GLOBAL BURDEN OF VIRAL LOWER RESPIRATORY TRACT DISEASE

There are limited data on the healthcare burden of lower respiratory tract disease (LRTD), particularly outside the United States. Pratik Sinha (Washington University School of Medicine, St. Louis, Missouri) presented an elegant study<sup>1</sup> using Bayesian modeling to estimate the global incidence of viral LRTD worldwide between 2010–2021. Not surprisingly, data from 2020–2021 reflected the tremendous impact of COVID-19, with total hospitalizations rising from 123 per 100,000 person years pre-pandemic to 388 per 100,000 person years. Yet even before the pandemic, annual increases in viral LRTD-related hospitalizations were documented, with 90 million hospitalizations cumulatively between 2010–2019. The healthcare burden of viral LRTD, many of which are vaccine preventable, underscores the importance of global surveillance for early detection, implementation of preventive strategies, and expedited administration of antiviral therapy.

Another multi-national study analyzed seasonality of influenza and COVID-19 in

the United States, United Kingdom, and European Union in the post-pandemic era.<sup>2</sup> This study, performed during the 2022–2023 and 2023–2024 seasons, found that influenza virus hospitalizations, which had diminished significantly during the pandemic, have returned to pre-pandemic levels. While influenza-related hospitalizations peak during winter months, there is less seasonality with SARS-CoV-2 hospitalizations. These findings highlight the need for maximizing coverage for both vaccine-preventable diseases.

## THE EMERGING THREAT OF HIGHLY PATHOGENIC AVIAN INFLUENZA VIRUSES

The looming threat of highly pathogenic avian influenza (H5N1) was a hot topic, with H5N1 dominating the Opening Plenary Session on Navigating the Next Pandemic.<sup>3</sup> The John Enders Lecture, presented by Tim Uyeki from the Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases focused on this emerging pathogen.<sup>4</sup> While human cases of H5N1 have been recognized

since 1997, primarily in Asia and Africa, the current Clade 2.3.4.4b H5N1 virus is displaying several unique features that raise the threat level of an evolving pandemic.

So far in 2024, there have been 25 human cases of H5N1 in the United States, in contrast to a solitary case in the preceding 2 years. In all but one of these cases, there was an epidemiologic link to an animal reservoir. While infection in poultry has been well documented, a novel feature in the US is the association of human cases with infected dairy cattle. Clade 2.3.4.4b H5N1 virus has also been detected in other zoonotic hosts and is a cause of significant mortality to livestock and wild animals. Reassuringly, there are no documented cases of human-to-human transmission among US cases, although in a single patient no zoonotic exposure was documented, and the source of infection remains unknown.

The clinical presentation of the Clade 2.3.4.4b H5N1 virus also appears to be unique from that seen in previous years. Historically, H5N1 presents as a respiratory illness, with manifestations ranging from mild disease to severe pneumonia. The case fatality of H5N1 infections between 1997–2024 approached 50%. In contrast, hemorrhagic conjunctivitis has been the presenting symptom in all but one of the 2024 US cases, and there have been no fatalities. Yet the fact that human cases in

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the US have been relatively mild should not be met with complacency. Viral mutations have the potential to allow human-to-human transmission, which in a non-immune population could have catastrophic consequences.

Virologic and disease surveillance are key measures to monitor H5N1 activity. Alessandro Zulli (Stanford University, Stanford, California) presented a timely oral abstract<sup>5</sup> outlining the utility of wastewater surveillance for identifying disease outbreaks. He and his colleagues reported on an investigation following detection of an out-of-season increase in influenza A concentrations in wastewater in Amarillo, Texas. Sequencing confirmed that this was



due to H5N1 virus, and the authors were able to localize the source to a specific dairy processing plant. Notably, viral detection in wastewater predated confirmed bovine and human cases by approximately 1 month, suggesting that testing of material from sewage treatment facilities may serve as a sentinel surveillance system for zoonotic infections and community transmission.

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## RESPIRATORY SYNCYTIAL VIRUS IMMUNIZATION IN ADULTS

Respiratory syncytial virus (RSV), long known to be a pathogen in young children, is now increasingly recognized to cause serious disease in older adults and those with medical comorbidities. This led the CDC Advisory Committee on Immunization Practices (ACIP) to recommend universal RSV vaccination among adults 60 years and older in June 2023 (later revised in June 2024 to age 75 and older).

A year into the approval of two RSV vaccines (RSV vaccine bivalent and RSV vaccine adjuvanted) for use in adults, post-marketing data was presented at IDWeek. Heidi Ransohoff (Los Angeles Department

of Public Health, Los Angeles, California) reported a study<sup>6</sup> by the Los Angeles County Department of Public Health evaluating the real-world efficacy of vaccination in elderly adults. During the study period, they identified almost 2,300 incident cases of RSV in adults aged 60 and older. Cross-linking these cases with the vaccine registry, the authors reported that the risk of RSV infection among unvaccinated individuals in the target population was 5.1 times higher than among the vaccinated cohort, providing compelling data supporting vaccine efficacy.

H. Keipp Talbot (Vanderbilt University, Nashville, Tennessee) presented data on FDA post-licensure adverse event monitoring for these two vaccines.<sup>7</sup> Among the more than 2 million adults who had received the RSV vaccine, there were 24 cases of Guillain-Barré syndrome. Using positive predictive value adjusted analysis, this translated to a risk of 10–25 cases per million doses. While elevated incidence of Guillain-Barré syndrome was only statistically significant for one of the vaccines, Talbot urged caution in directly comparing the side effect profile due to the small numbers of patients affected.

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