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Literature review

Respiratory viruses

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Volume 29, Number 3—March 2023

Research

Using Discarded Facial Tissues to Monitor and Diagnose Viral Respiratory Infections

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Abstract

Molecular biology amplification enables sensitive detection of most respiratory viruses through nasopharyngeal swabbing. We developed an innovative approach to detect viral genomes on used facial tissues. In 2 communities of children, used tissues were collected once weekly for 1 year. Pooled analysis of tissues enabled detection of successive virus circulation in 4 age groups over time and forecasted by several weeks the circulation of influenza in the general population. At the individual level, in a proof-of-concept study of 30 volunteers with influenza-like signs/symptoms, we identified common respiratory viruses. The signals for SARS-CoV-2 obtained in parallel from 15 facial tissues and swab samples were similar and often higher for the tissues (11/15). Individual analysis of tissues offers a noninvasive, sensitive, and affordable alternative to self-sampling without a medical care requirement. Pooled analyses may be used to detect virus spread in specific communities, predict seasonal epidemics, and alert the population to viral infections.

Respiratory viral infections (RVIs) are the most common virus-induced pathologies. Associated signs/symptoms range from common colds with simple rhinorrhea without fever to acute respiratory distress syndrome sometimes leading to death ([1](#)). In addition to their clinical effects, RVIs have a major economic effect because of not only healthcare resource use (direct costs) but also productivity losses (indirect costs), and they paradoxically receive little attention ([2,3](#)). Moreover, antimicrobial treatments are too often prescribed for RVIs, thereby disseminating antimicrobial resistance.

Methods

1. Collected pooled facial tissues from children in daycare during 27 weeks of winter 2018-19
2. Collected pooled facial tissues from preschool children during 25 weeks of winter 2019-20
3. Collected individual samples as soon as they exhibited influenza-like signs/symptoms from 22 children

For pooled samples, tissues were counted and pooled specimens eluted with 7 mL of DPBS per tissue (gently soaked for few minutes then pressed with a “home-brew device”)

“Individual collections” were also eluted with 7ml DPBS in a 60-mL syringe, then the syringe plunger firmly pressed down - regularly obtained 5 mL of liquid.



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Methods

For pooled sample testing:

Allplex Seegene

influenza A; influenza A(H1); influenza A(H1N1)pdm09;
influenza A(H3); influenza B; RSV A and B; adenovirus;
enterovirus; hMPV; PIV 1–4; bocaviruses 1–4; CoV 229E, NL63,
and OC43; and hRhV

For individual testing:

TaqPath, Alinity, GeneXpert, and FilmArray.

To detect CMV, EBV and human parvovirus B19

RealStar assays



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Results Phase 1



Figure 1. From cited paper – pooled samples from daycare groups. Each week is represented by a column, and detection of different viruses is indicated by a crossed cell. O, older age group; Y, younger age group.

Lagathu G, Grolhier C, Besombes J, Maillard A, Comacle P, Pronier C, et al. Using Discarded Facial Tissues to Monitor and Diagnose Viral Respiratory Infections. *Emerg Infect Dis.* 2023;29(3):511-518. <https://doi.org/10.3201/eid2903.221416>



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Results Phase 3

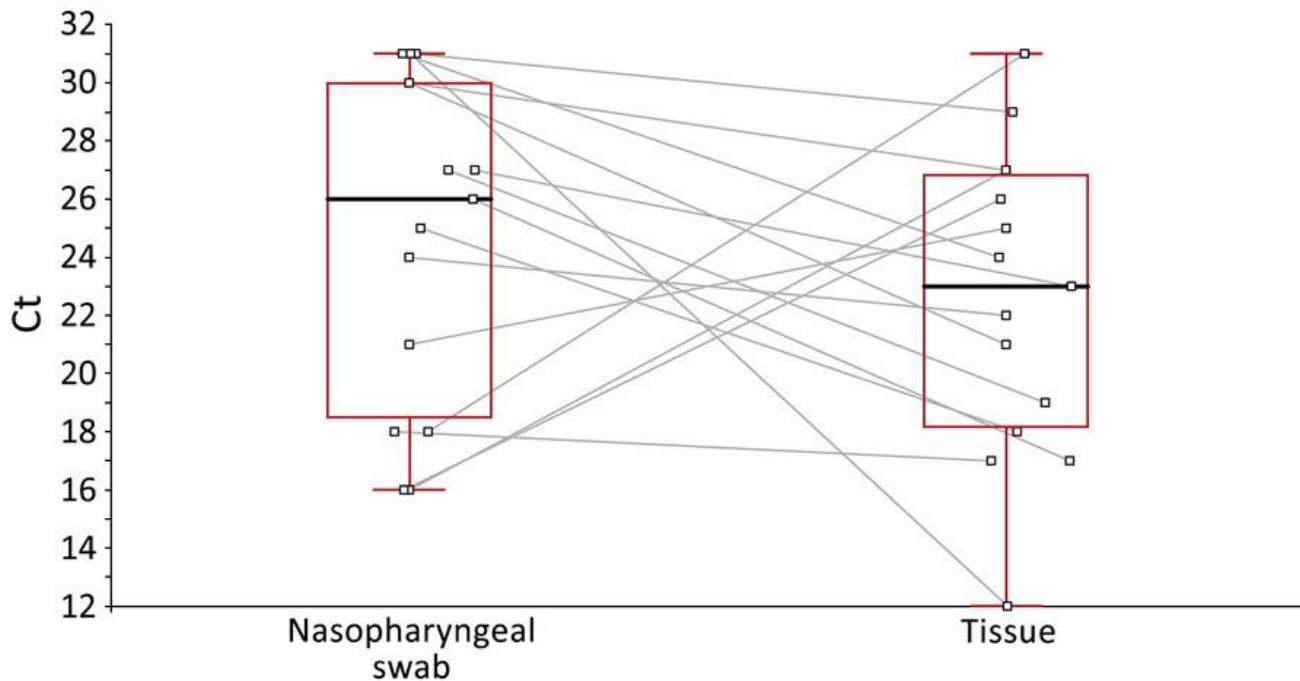


Figure 3. Reverse transcription PCR signal (Ct) obtained from nasopharyngeal swab samples collected from persons with COVID-19 compared with Ct obtained from processed used facial tissues in study of using facial tissues to monitor and diagnose viral respiratory infection. Each square indicates a patient, and observations for the same patient are linked between plots. Black lines within boxes indicate medians; box tops, 75th percentile; box bottoms, 25th percentile; and whiskers, maximums and minimums. Ct, cycle threshold.

Long COVID: major findings, mechanisms and recommendations

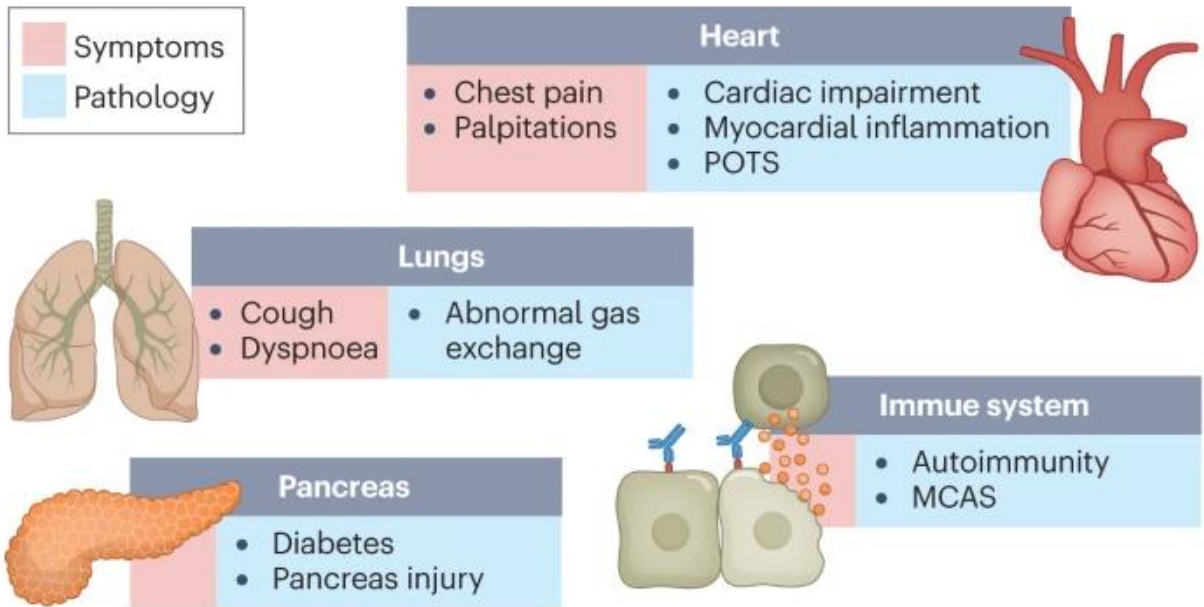
[Hannah E. Davis](#), [Lisa McCorkell](#), [Julia Moore Vogel](#) & [Eric J. Topol](#) 

Nature Reviews Microbiology **21**, 133–146 (2023) | [Cite this article](#)

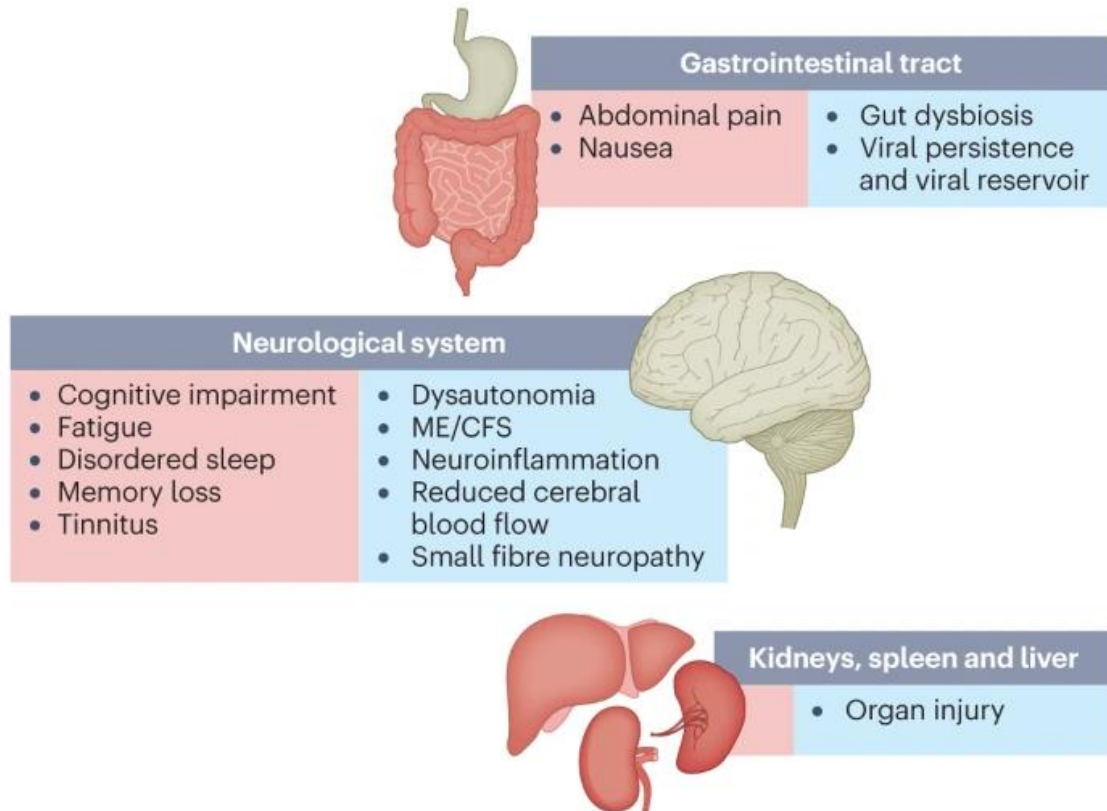
691k Accesses | **19** Citations | **10389** Altmetric | [Metrics](#)

Abstract

Long COVID is an often debilitating illness that occurs in at least 10% of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections. More than 200 symptoms have been identified with impacts on multiple organ systems. At least 65 million individuals worldwide are estimated to have long COVID, with cases increasing daily. Biomedical research has made substantial progress in identifying various pathophysiological changes and risk factors and in characterizing the illness; further, similarities with other viral-onset illnesses such as myalgic encephalomyelitis/chronic fatigue syndrome and postural orthostatic tachycardia syndrome have laid the groundwork for research in the field. In this Review, we explore the current literature and highlight key findings, the overlap with other conditions,

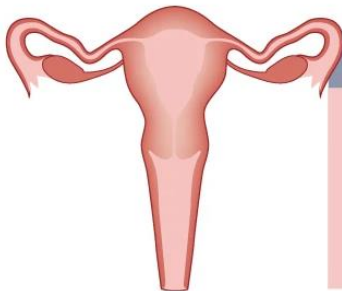


From Figure 1 in Davis et al. (2023): Nature Reviews Microbiology 21: 133-146



From Figure 1 in Davis et al. (2023): Nature Reviews Microbiology 21: 133-146

Blood vessels	
• Fatigue	• Coagulopathy • Deep vein thrombosis • Endothelial dysfunction • Microangiopathy • Microclots • Pulmonary embolism • Stroke



Reproductive system	
• Erectile dysfunction • Increased severity and number of premenstrual symptoms • Irregular menstruation	• Reduced sperm count



Original Investigation | Infectious Diseases

Prevalence and Correlates of Long COVID Symptoms Among US Adults

Roy H. Perlis, MD, MSc; Mauricio Santillana, PhD; Katherine Ognyanova, PhD; Alauna Safarpour, PhD; Kristin Lunz Trujillo, PhD; Matthew D. Simonson, PhD; Jon Green, PhD; Alexi Quintana, BA; James Druckman, PhD; Matthew A. Baum, PhD; David Lazer, PhD

Abstract

IMPORTANCE Persistence of COVID-19 symptoms beyond 2 months, or long COVID, is increasingly recognized as a common sequela of acute infection.

OBJECTIVES To estimate the prevalence of and sociodemographic factors associated with long COVID and to identify whether the predominant variant at the time of infection and prior vaccination status are associated with differential risk.

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional study comprised 8 waves of a nonprobability internet survey conducted between February 5, 2021, and July 6, 2022, among individuals aged 18 years or older, inclusive of all 50 states and the District of Columbia.

MAIN OUTCOMES AND MEASURES Long COVID, defined as reporting continued COVID-19 symptoms beyond 2 months after the initial month of symptoms, among individuals with self-reported positive results of a polymerase chain reaction test or antigen test.

RESULTS The 16 091 survey respondents reporting test-confirmed COVID-19 illness at least 2 months prior had a mean age of 40.5 (15.2) years; 10 075 (62.6%) were women, and 6016 (37.4%) were men; 817 (5.1%) were Asian, 1826 (11.3%) were Black, 1546 (9.6%) were Hispanic, and 11 425 (71.0%) were White. From this cohort, 2359 individuals (14.7%) reported continued COVID-19

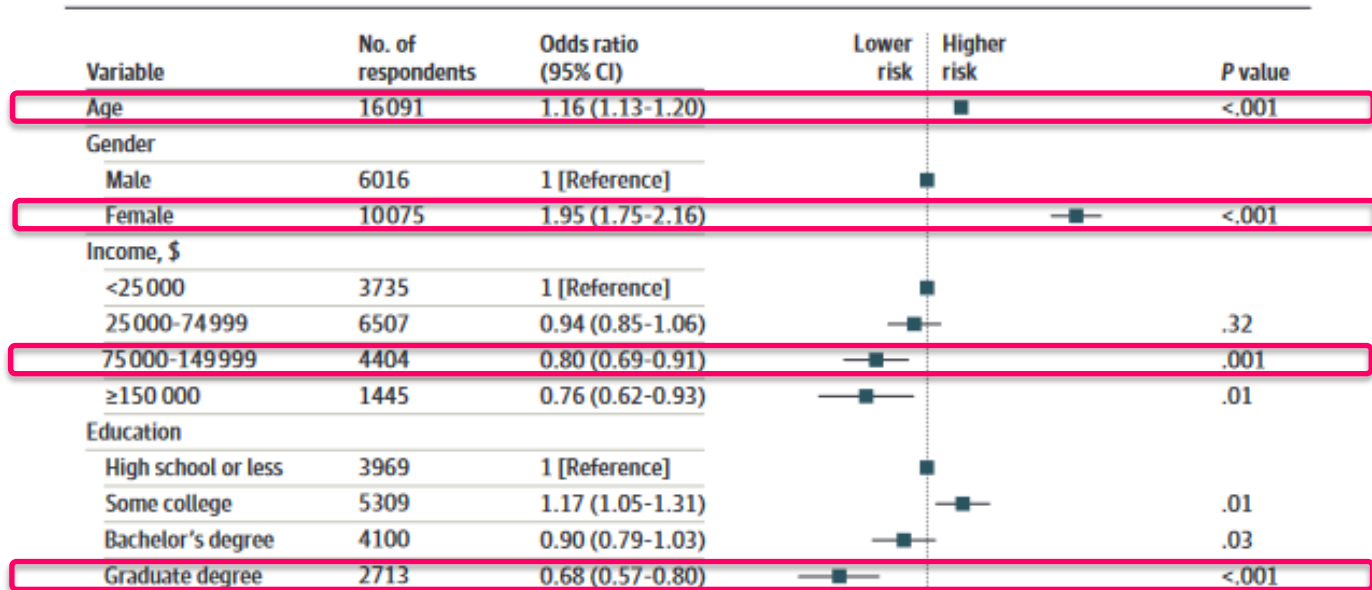
Key Points

Question How common are COVID-19 symptoms lasting longer than 2 months, also known as *long COVID*, among adults in the United States, and which adults are most likely to experience long COVID?

Findings In this cross-sectional study of more than 16 000 individuals, 15% of US adults with a prior positive COVID-19 test reported current symptoms of long COVID. Those who completed a primary vaccination series prior to infection were less likely to report long COVID symptoms.

Meaning This study suggests that long COVID is prevalent and that the risk varies among individual subgroups in the United States; vaccination may

Figure 2. Logistic Regression Model for Development of Long COVID Among Individuals Testing Positive for COVID-19 by Antigen Test or Polymerase Chain Reaction Test, Including Predominant Variant and Vaccination Status at Time of Infection

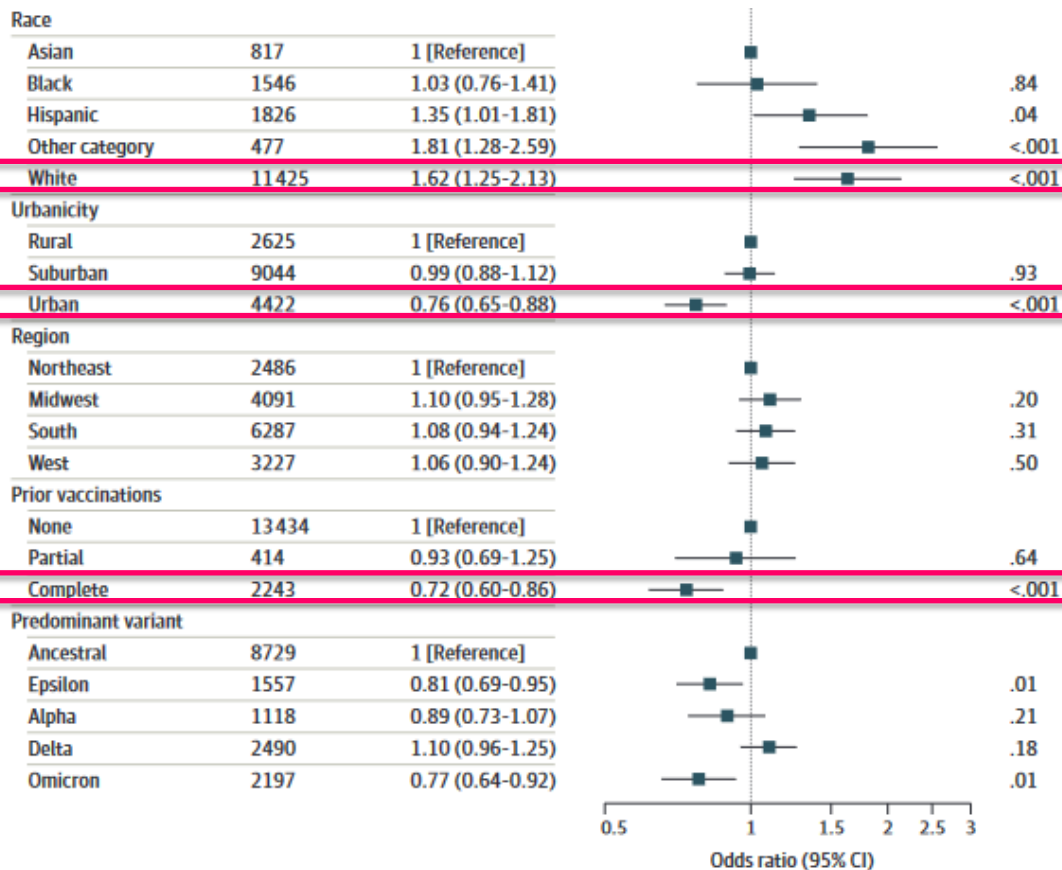


From Figure 2 in Perlis et al. 2022 JAMA Netw Open. 5(10):e2238804



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From Figure 2 in Perlis et al. 2022 JAMA Netw Open. 5(10):e2238804



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Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults

Alberto Papi, M.D., Michael G. Ison, M.D., Joanne M. Langley, M.D., Dong-Gun Lee, M.D., Ph.D., Isabel Leroux-Roels, M.D., Ph.D., Federico Martinon-Torres, M.D., Ph.D., Tino F. Schwarz, M.D., Ph.D., Richard N. van Zyl-Smit, M.D., Ph.D., Laura Campora, M.D., Nancy Dezutter, Ph.D., Nathalie de Schrevel, Ph.D., Laurence Fissette, M.S., *et al.*, for the AReSVi-006 Study Group*

Abstract

BACKGROUND Respiratory syncytial virus (RSV) is an important cause of acute respiratory infection, lower respiratory tract disease, clinical complications, and death in older adults. There is currently no licensed vaccine against RSV infection.

METHODS In an ongoing, international, placebo-controlled, phase 3 trial, we randomly assigned, in a 1:1 ratio, adults 60 years of age or older to receive a single dose of an AS01_E-adjuvanted RSV prefusion F protein-based candidate vaccine (RSVPreF3 OA) or placebo before the RSV season. The primary objective was to show vaccine efficacy of one dose of the RSVPreF3 OA vaccine against RSV-related lower respiratory tract disease, confirmed by reverse-transcriptase polymerase chain reaction (RT-PCR), during one RSV season. The

February 16, 2023

N Engl J Med 2023; 388:595-608

DOI: 10.1056/NEJMoa2209604

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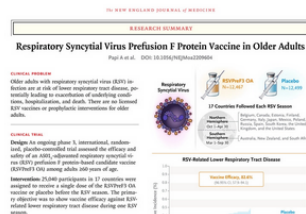
PERSPECTIVE FEB 16, 2023

The Journey to RSV Vaccines — Heraldizing an Structure-Based Design

B.S. Graham

ORIGINAL ARTICLE FEB 16, 2023

Efficacy and Safety of an Ad26.RSV.preF-RS Protein Vaccine in Older Adults



Trial description

- ongoing, international, placebo-controlled, phase 3 trial
- 1:1 ratio, ≥ 60 yo
- single dose adjuvanted RSV prefusion F protein–based candidate vaccine or placebo before RSV season
- median follow-up 6.7 months
- primary objective - show vaccine efficacy of one dose, against RT-PCR-confirmed, RSV-related lower respiratory tract disease



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Results

- Participants: vaccine - 12,467; placebo - 12,499
- Efficacy against RT-PCR–confirmed RSV-related lower respiratory tract disease 82.6%:
 - 7 cases in vaccine group, 40 cases in placebo group
- Vaccine efficacy:
 - 94.1% against severe RSV-related LRT Dx
 - 71.7% against RSV-related acute respiratory infection
 - Similar against the RSV A and B subtypes
 - High efficacy observed in participants with coexisting conditions
- Vaccine was more reactogenic than placebo, but most adverse events were transient, with mild-to-moderate severity
- Serious adverse events and potential immune-mediated diseases were similar in the two groups

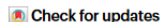


Coinfection by influenza A virus and respiratory syncytial virus produces hybrid virus particles

Received: 10 August 2021

Accepted: 2 September 2022

Published online: 24 October 2022



Joanne Haney¹, Swetha Vijayakrishnan¹, James Streetley², Kieran Dee¹, Daniel Max Goldfarb¹, Mairi Clarke², Margaret Mullin³, Stephen D. Carter¹, David Bhella^{1,2} and Pablo R. Murcia¹✉

Interactions between respiratory viruses during infection affect transmission dynamics and clinical outcomes. To identify and characterize virus–virus interactions at the cellular level, we coinfect human lung cells with influenza A virus (IAV) and respiratory syncytial virus (RSV). Super-resolution microscopy, live-cell imaging, scanning electron microscopy and cryo-electron tomography revealed extracellular and membrane-associated filamentous structures consistent with hybrid viral particles (HVPs). We found that HVPs harbour surface glycoproteins and ribonucleoproteins of IAV and RSV. HVPs use the RSV fusion glycoprotein to evade anti-IAV neutralizing antibodies and infect and spread among cells lacking IAV receptors. Finally, we show that IAV and RSV coinfection in primary cells of the bronchial epithelium results in viral proteins from both viruses co-localizing at the apical cell surface. Our observations define a previously unknown interaction between respiratory viruses that might affect virus pathogenesis by expanding virus tropism and enabling

An airway-to-brain sensory pathway mediates influenza-induced sickness

[Na-Ryum Bin](#), [Sara L. Prescott](#), [Nao Horio](#), [Yandan Wang](#), [Isaac M. Chiu](#) & [Stephen D. Liberles](#) 

[Nature](#) (2023) | [Cite this article](#)

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Abstract

Pathogen infection causes a stereotyped state of sickness that involves neuronally orchestrated behavioural and physiological changes^{1,2}. On infection, immune cells release a ‘storm’ of cytokines and other mediators, many of which are detected by neurons^{3,4}; yet, the responding neural circuits and neuro-immune interaction mechanisms that evoke sickness behaviour during naturalistic infections remain unclear. Over-the-counter medications such as aspirin and ibuprofen are widely used to alleviate sickness and act by blocking prostaglandin E2 (PGE2) synthesis⁵. A leading model is that PGE2 crosses the blood-brain barrier and directly engages hypothalamic neurons². Here, using genetic tools that broadly cover a peripheral sensory neuron atlas, we instead identified a small population of PGE2-detecting glossopharyngeal sensory neurons (petrosal GABRA1 neurons) that are essential for influenza-induced sickness behaviour in mice. Ablating petrosal GABRA1 neurons or targeted knockout of PGE2 receptor 3 (EP3) in these neurons eliminates influenza-induced

Evidence for an aquatic origin of influenza virus and the order *Articulavirales*

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ABSTRACT

The emergence of novel disease-causing viruses in mammals is part of the long evolutionary history of viruses. Tracing these evolutionary histories contextualises virus spill over events and may help to elucidate how and why they occur. We used a combination of total RNA sequencing and transcriptome data mining to extend the diversity and evolutionary history of the order *Articulavirales*, which includes the influenza viruses. From this, we identified the first instance of *Articulavirales* in the Cnidaria (including corals), constituting a novel and divergent family that we tentatively named the *Cnidenomoviridae*. This may be the basal group within the *Articulavirales*. We also extended the known evolutionary history of the influenza virus lineage by identifying a highly divergent, sturgeon-associated influenza virus. This suggests that fish were among the first hosts of influenza viruses. Finally, we substantially expanded the known diversity of quaranjaviruses and proposed that this genus be reclassified as a family (the *Quaranjaviridae*). We find evidence that vertebrate infecting *Quaranjaviridae* may have initially evolved in crustaceans before spilling into terrestrial Chelicerata (i.e., ticks). Together, our findings indicate that the *Articulavirales* has evolved over at least 600 million years, first emerging in aquatic animals. Importantly, the evolution of this order was not shaped by strict virus-host codivergence, but rather by multiple aquatic-terrestrial transitions and substantial host jumps, some of which are still observable today.

Sincere thanks to

Sara Griesemer
Jennifer Laplante

Laboratory of Viral Diseases
Wadsworth Center



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