



INFECTIOUS DISEASE

Collateral effects of pandemic control

The response to COVID-19 altered global dispersal of influenza viruses

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Influenza accounts for an estimated 500,000 global deaths annually (1). Although vaccines are available to protect individuals from infection and severe disease, their protectiveness varies from season to season (2). This is largely because of rapid viral evolution in response to infection- and vaccine-derived immunity, which leads to the sporadic and hard-to-predict emergence of antigenically new viruses that can bypass existing immunity (3, 4). Another complexity lies in the multiple geographic locations that may serve as evolutionary reservoirs and seed subsequent epidemics in different parts of the world (4, 5). Non-

the spread of SARS-CoV-2. These actions had a profound impact on influenza transmission (see the figure). Seasonal influenza cases—caused by subtype A viruses H1N1 and H3N2 and subtype B viruses Victoria and Yamagata—plummeted globally during the pandemic, illustrating the power of nonpharmaceutical interventions to reduce the spread of respiratory pathogens. Chen *et al.* sought to understand how localized viral evolution and disruptions in human movement act in concert to shape the global spread and transmission dynamics of these viruses. The authors defined three distinct time periods—the prepandemic, pandemic, and postpandemic—using data on air travel and the severity of pandemic response, as

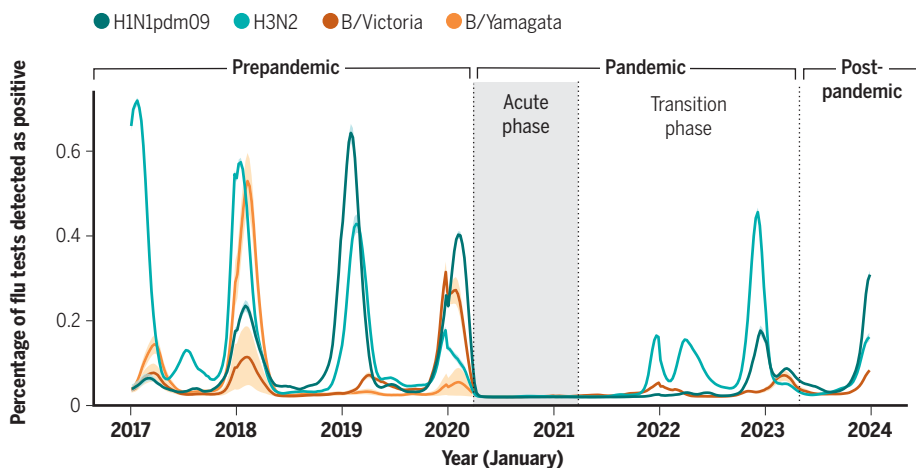
reductions in international air travel, Chen *et al.* found that air passenger traffic was still a strong predictor of global influenza dissemination (9), depending on local transmission intensity at the population of origin. By 2023–2024, viral diffusion among regions had reverted largely to prepandemic levels. A notable advantage of the study's methodology is the ability to identify which geographic regions served as the evolutionary source of influenza viruses, referred to as the phylogenetic trunk location. The authors report that during the pandemic, South Asia (India, Iran, and Bhutan) played an outsized role in generating influenza A viral branches that persisted across seasons, whereas West Asia (Armenia, Azerbaijan, Bahrain, Georgia, Israel, Lebanon, Oman, Qatar, and Saudi Arabia) maintained the circulation of the B/Victoria strain.

One of the consequences of introducing new influenza viruses into a geographic region is the competition with, and subsequent local extinction of, existing viruses in the recipient population. This phenomenon is quantified by estimating the length of time that a lineage spends in each location, which is called the dwell time. In the prepandemic period, dwell times for H3N2 viruses were estimated to be approximately 6 months. However, in the acute phase of the pandemic, there was reduced strain replacement, leading to increased lineage-associated dwell times. These patterns reflect a reduction in viral movement due to less frequent long-distance travel. Notably, the Chen *et al.* study identifies an important role for Africa and West Asia in maintaining the B/Victoria virus during the acute phase of the pandemic, with dwell times for all four influenza viruses longer in Africa than in other regions.

A striking finding by Chen *et al.* is the prolonged absence of the influenza B/Yamagata strain since the start of the pandemic. The authors propose that it might be due to a mixture of susceptible host depletion (there was a large outbreak of B/Yamagata in 2017–2018), the pandemic-induced rapid changes in human behavior and movement, and the previously documented minimal antigenic evolution of

Global influenza activity across pandemic periods

Standardized influenza activity of H1N1, H3N2, B/Victoria, and B/Yamagata was determined by Chen *et al.*



pharmaceutical interventions such as social distancing, mask wearing, hand hygiene, and travel restrictions can provide an additional layer of defense. The COVID-19 pandemic provided an unexpected natural experiment to evaluate the effectiveness of these measures on influenza. On page 639 of this issue, Chen *et al.* (6) report how nonpharmaceutical COVID-19 pandemic control efforts reshaped the global dispersal of influenza.

Many countries implemented stringent nonpharmaceutical interventions to reduce

quantified by the “stringency index” developed by the Oxford COVID-19 Government Response Tracker (7). Using a phylodynamic approach (8) that simultaneously considers a combination of international travel data, viral genome sequences, and influenza incidence reports, the authors paint a compelling picture of how changes in human behavior influenced the global transmission and evolution of influenza viruses.

Although the acute phase of the pandemic was associated with considerable

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the surface hemagglutinin glycoprotein that is essential for viral infectivity (10, 11). The potential extinction of this lineage has public health implications, as evidenced by the recommendation of trivalent vaccines (which exclude the B/Yamagata strain) in the Northern Hemisphere for the 2024–2025 season.

The study by Chen *et al.* further reinforces that nonpharmaceutical interventions can be incredibly effective in disrupting viral transmission, pathogen diversity, and antigenic evolution, and are arguably more effective than vaccination efforts alone. The authors also point to possible longer-term impacts of the COVID-19 pandemic on influenza ecology and evolution. The reported increases in dwell times of seasonal influenza lineages indicate a shift in the intensity of antigenic competition among strains. Longer dwell times may lead to increased regional viral diversification and the emergence of spatially structured antigenic variants, increasing the risk of mismatch with vaccines in recipient populations. In addition, the pandemic fundamentally altered the influenza immune landscape through a combination of much lower levels of natural infection and interruption of seasonal vaccination programs. The reduced population-level immunity could contribute to subsequent larger influenza epidemics like the 2023 outbreak in Hong Kong (12).

One possible extension of the study of Chen *et al.* is to adopt multiscale phylogenetic modeling that simultaneously considers viral evolution, mobility, and transmission dynamics to unravel the cause-and-effect relationships between age-structured contacts (13), age-specific patterns of mobility (14), and antigenic trajectories. This information can strategically inform how vaccination efforts can be combined with nonpharmaceutical interventions to disrupt the virus life cycle and more effectively control the burden of influenza infection and disease. ■

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CHEMICAL SEPARATION

A two-faced membrane channel

Contrasting surface properties activate a feedback loop system for a complete oil-and-water separation

By Xing Yang and
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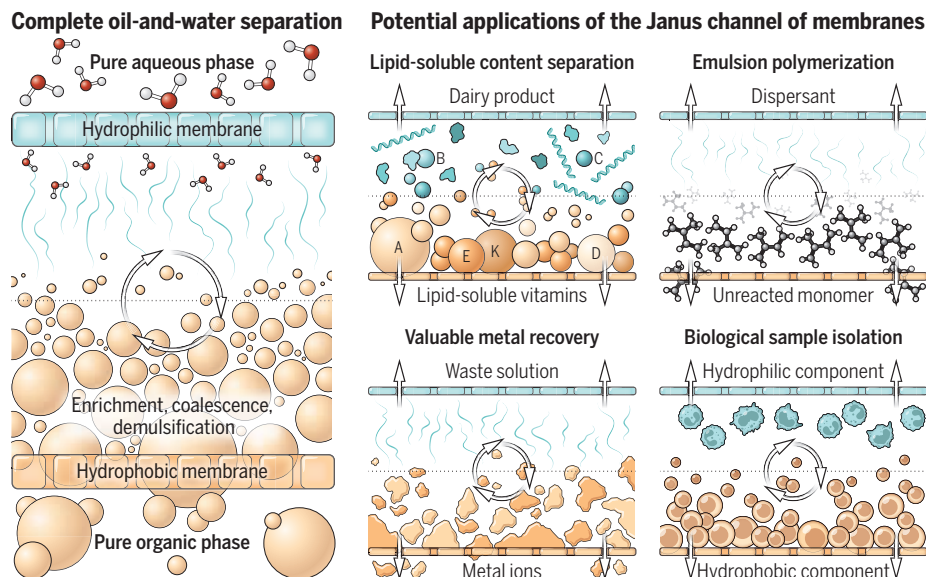
From treating wastewater to sorting biological components, the separation of oil and water from a complex mixture is relevant to processes across many industries and branches of science. Membranes are key components to separation techniques such as reverse osmosis, which is used to purify water. However, traditional membrane technologies are often limited to filtering only one component from a mixture, leaving the remaining liquid highly concentrated with residues such as salts and organic matter (1). This not only makes further separation challenging by increasing the thermodynamic stability of the materials left behind in the solution but also creates potential disposal hazards. On page 654 of this issue, Guo *et al.* (2) report the ingenious design of a membrane system that can simultaneously separate oil and water in a single stream from a surfactant-stabilized mixture. This strategy could be combined with other commercial

membranes for a breadth of applications.

Guo *et al.* designed a Janus channel of membranes, which is named after the two-faced Roman god Janus—who represents a simultaneous duality—because the membrane system consists of a narrow channel (width of ~0.4 mm) between two membranes of opposing wetting properties, that is, differing abilities for a liquid to maintain contact with a solid surface. One side of the channel is hydrophilic (water-loving), whereas the other side has a hydrophobic (water-hating) membrane. The feed emulsion moves parallel to the surfaces of both membranes. External pressure from the influx of solution generates strong chemical affinity between water molecules and the hydrophilic surface. Water passes through the membrane and leaves behind an oil-enriched emulsion in the channel. Consequently, as the density of oil droplets further increases, it activates the hydrodynamic aspects (forces exerted by moving fluid) inside the channel, which increases the collision frequency between oil droplets within the mixture. This facilitates the

Janus channel of membranes with a feedback loop

A stabilized mixture passes through a narrow channel with two membranes of opposing surface properties. As water is filtered through the hydrophilic side, the increased density of small oil droplets in the channel enables coalescence and demulsification of the organic phase through the hydrophobic side. A continuous inlet of mixture creates a feedback-loop system until a complete separation is achieved.



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