



Vaccine 'breakthrough infections' with SARS-CoV-2

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Game plan

- ▶ Review a few recent articles on SARS-CoV-2 infections among people who have been fully vaccinated...including discussion of the definition of 'breakthrough infection'
- ▶ Examine results from a NY Times survey of 723 epidemiologists on their perspectives of Covid-19 and the future of the pandemic

Objectives

- ▶ Write a viable definition of 'breakthrough infections'
- ▶ State what is known/not known about transmission of virus among people who are vaccinated
- ▶ Summarize key perspectives from an epidemiologic survey of epidemiologists
- ▶ Pass a quiz at the end

Take home messages

- ▶ The definition of SARS-CoV-2 'breakthrough infection' is not consistently agreed upon and in most articles, appears to mean 'vaccine failure'—which is expected in a small % of vaccinees
- ▶ Recovery of SARS-CoV-2 from nasal mucosa or from salivary samples appears to be common among vaccinated people
- ▶ A mucosal vaccine that induces tissue-resident immune cells will be very useful to block transmission
- ▶ The needed data that address transmission risk for test-positive fully vaccinated people, are currently not yet available
- ▶ Many epidemiologists in the US express different opinions about the most important control strategies and the future of the pandemic, although some common themes emerge from a recent survey


Introduction

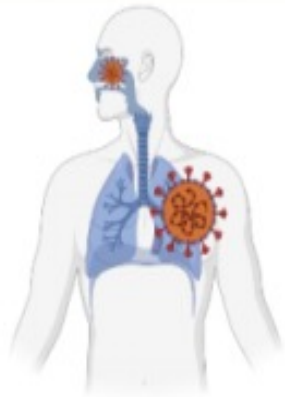
- ▶ Substantial amount of news coverage on vaccine failure or 'breakthrough infections' among different vaccinated groups in US and abroad
- ▶ Given results of the large vaccine trials, we should not be too surprised about this observation (efficacy NOT 100%)
- ▶ Even the NY Yankees are not excluded from vaccine failures (by the common definition, i.e., PCR-positive results from a nasal swab or salivary test, among individuals post vaccination)
- ▶ Few published data exist on Covid breakthrough (or vaccine failure) in tribal people in US, or anywhere else, tho a regional tribe reported 18 such cases recently (moderately sized tribe) and another regional tribal clinician observed cases in a smaller NW tribe

Immune response to vaccines

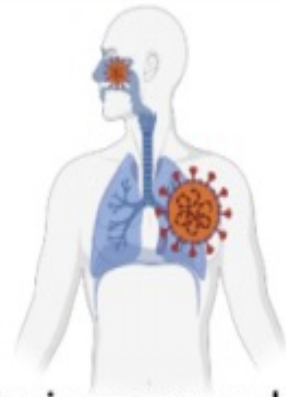
(Schieffelin, 2021)

- ▶ Current SARS-CoV-2 vaccines provide anti-spike IgG response and T cell response
- ▶ Little data on resident memory B cells (that produce antibodies) or T cells from the current IM vaccines...particularly relevant to nasal mucosa in this discussion
- ▶ Recall that *S. pneumonia* vaccine prevents meningitis but not nasal colonization
- ▶ Also, that anti-RSV monoclonal antibody prevents most hospitalization for RSV pneumonia, but does not fully block transmission
- ▶ Further, seasonal flu vaccine produces high level of antibodies, but does not fully prevent transmission
- ▶ Nasal adenovirus vaccine more effective at reducing viral load in resp tract, compared to IM vaccination in a recent study

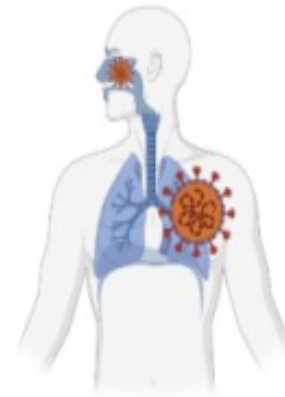
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- ▶ The authors conclude in this editorial that IgG antibodies acquired from IM injection would have little effect on nasal infection, nasal carriage, and nasal shedding of SARS-CoV-2
 - ▶ In absence of 100% vaccination coverage, they suggest continued current mitigation strategies (maybe I should say 'former mitigation strategies' given recent announcements)
 - ▶ Unless safe mucosal vaccines are developed that act in the appropriate target tissues (like nasal mucosa and upper/lower respiratory tract), we need to be cautious.



**Vaccine non-responder
(PCR+, LRI)**



**Vaccine poor responder/
ineffective responses to
new variant
(PCR+, LRI)**



**Vaccine responder
(PCR+, LRI)**



**Vaccine responder
(PCR+, asymptomatic)**

Immune response to vaccine	no	variable	yes	yes
Immune response to virus	variable	variable	yes	yes
Nasal infection status	positive	positive	positive	positive
Lower respiratory infection (LRI)	yes	yes	yes	no
Likely transmission risk	high	high	high	moderate*
Disease status	yes clinical disease	yes clinical disease	yes clinical disease	asymptomatic/URI only
Breakthrough infection?	NO	YES	YES	NO




Figure 1. Clinical scenarios and proposed classification of breakthrough infection based on disease in lower respiratory track. We propose that breakthrough infection after COVID-19 vaccination is defined by evidence of lower respiratory tract infection (LRI) and a positive PCR test for SARS-COV-2. Vaccinated individuals who are asymptomatic or limited to upper respiratory tract infection (URI) do not constitute a breakthrough infection, although it is important to understand that these individuals can still transmit virus. We also suggest that those individuals who do not mount an effective immune response to vaccination do not represent cases of breakthrough infection.

*transmission risk likely proportionate to viral copy number.

Perhaps they are best classified as **post-vaccination upper respiratory tract infections** .

The formal criteria for a true breakthrough infection could include evidence of radiographic abnormalities, a widened alveolar-arterial (A-a) gradient, or hypoxemia defined by low oxygen saturations in the arterial blood by pulse oximetry. These criteria will be critical to determine which positive SARS-CoV-2 tests are true vaccine failures in the lower respiratory tract versus the upper respiratory tract. In the current environment of widespread vaccine hesitancy, these distinctions will be crucial to maintaining, and possibly increasing, the public's trust in vaccines as well as understanding the role of vaccination in ending the pandemic.

Postvaccination SARS-CoV-2 Infections Among Skilled Nursing Facility Residents and Staff Members — Chicago, Illinois, December 2020–March 2021

Weekly / April 30, 2021 / 70(17);632-638

On April 21, 2021, this report was posted online as an MMWR Early Release.

Richard A. Teran, PhD^{1,2*}; Kelly A. Walblay, MPH^{2*}; Elizabeth L. Shane, MPH²; Shannon Xydis²; Stephanie Gretsche, MPH³; Alexandra Gagner, MPH²; Usha Samala, MPH²; Hyeree Choi²; Christy Zelinski, MPH²; Stephanie R. Black, MD² ([View author affiliations](#))

Post-vaccination infections, MMWR, 2021

- ▶ 78 Chicago area skilled nursing home facilities, routine testing conducted on patients and staff
- ▶ 15,000 participants, almost 1/2 were staff
- ▶ Case def of 'breakthrough infection': a positive PCR or RT-PCR test >14 days after second vaccination


MMWR, cntd

- ▶ 22 persons found to meet breakthrough definition (many others diagnosed with COVID-19 were identified before the second vaccination occurred)
- ▶ 14 asymptomatic, 3 mild symptoms, 3 pneumonia cases, 2 hospitalized with COVID-19-related symptoms/signs, 1 death
- ▶ No evidence of secondary transmission within any facility
- ▶ Author's caveat: data are very limited on the risk of transmission of SARS-CoV-2 post vaccination, in congregate settings, such as nursing homes

Post vaccination infections in HCW's in Israel

(Angel et al, 2021)

- ▶ Single hospital in Tel Aviv
- ▶ 6700 health care workers followed for two months, not all were vaccinated
- ▶ Routine PCR-based testing/questionnaires
- ▶ Definitions: COVID-19 diagnosis >7 days after second Pfizer/BNT vaccine
- ▶ Symptomatic infection: IRR 0.03 vaccinated vs. unvaccinated
- ▶ Asymptomatic infection: IRR 0.14 vaccinated vs. unvaccinated
- ▶ Authors could not assess the transmission risk of asymptomatic, PCR positive cases to others



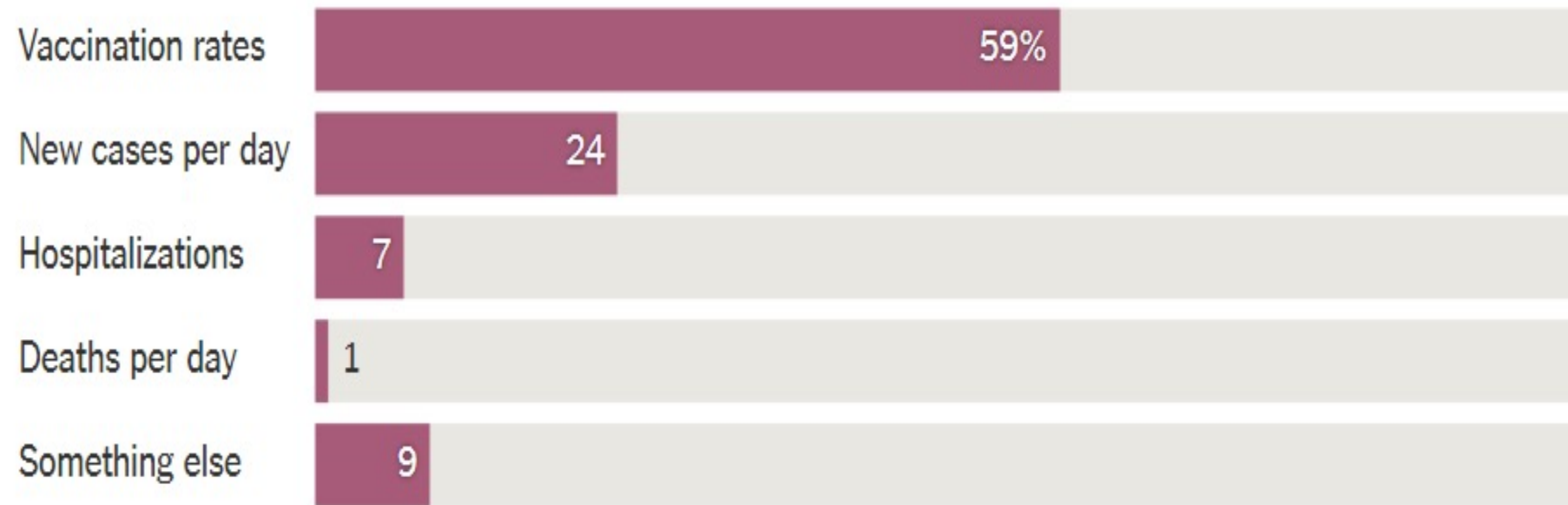
In those cases, "the resulting infection is more likely to have a lower viral load, may be shorter in duration, and likely less risk of transmission to others," said Dr. Rochelle Walensky, director of the US Centers for

Part 2: Survey of US epidemiologists

- ▶ NY Times conducted the survey, n=723
- ▶ Sampled Society of Epidemiologic Research and CSTE
- ▶ Primarily single choice-type questions
- ▶ Respondents mostly government workers and academics
- ▶ The participating epidemiologists were NOT a group of strictly infectious disease epi people

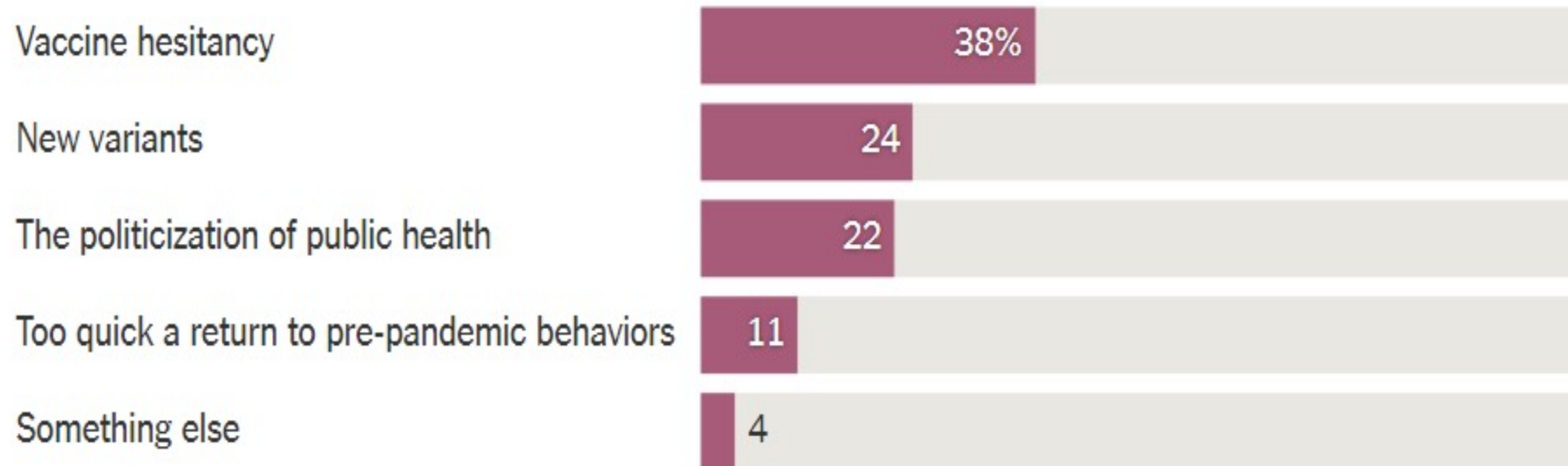
On the Most Relevant Covid-19 Metric for Reopening

Which statistic do you feel is most important in helping determine when we can resume most pre-pandemic activities without new Covid-era precautions?



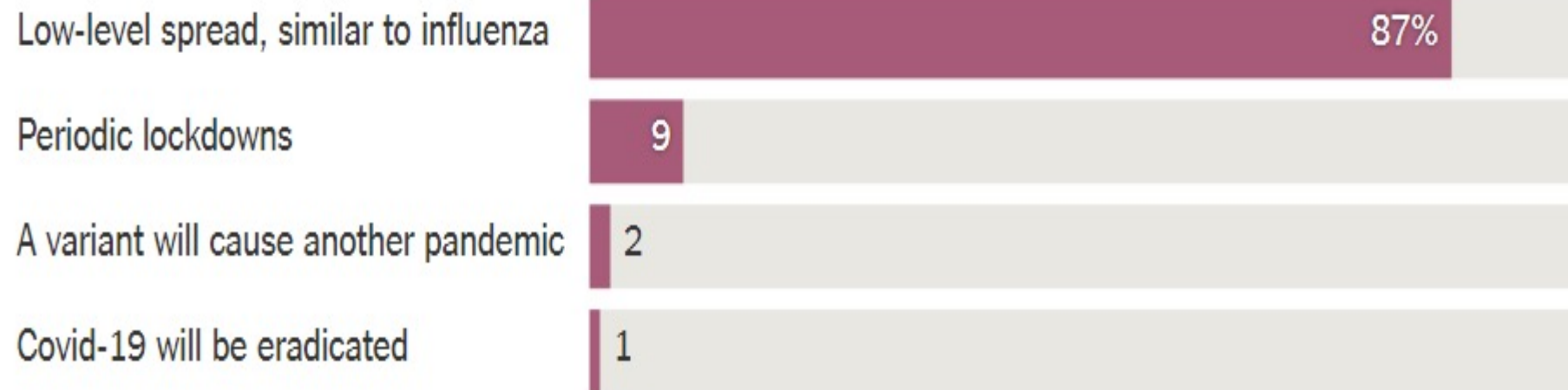
Potential Obstacles

If you had to pick one, what is the thing you most fear could stall progress toward ending this pandemic?



On What Covid-19 Might Be Like in 2026

Thinking around five years into the future, if you had to guess, what will the state of Covid-19 be in the United States?



Vaccine breakthrough-related Quiz

- ▶ One of the authors of an 'opinion article' or editorial suggested that successful (IgG response) vaccination followed by lower respiratory infection from SARS-CoV-2 is the 'correct way' to define breakthrough infections. Do you agree? Why or why not?
- ▶ If vaccine hesitancy is the single biggest factor affecting the course of this pandemic (per the NYT survey), what would be your plans to incentivize people to get vaccinated or otherwise drive up % of vaccinees?
- ▶ What do YOU think is the biggest obstacle to ending the pandemic if you were to participate in a survey like the NYT survey?

references

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- ▶ Grazie a Grazia Ori per la sua assistenza...ha trovato tutti.

Refs, cntd

- ▶ [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(21\)00224-3/fulltext#articleInformation](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00224-3/fulltext#articleInformation)_Vaccine effectiveness against variants in Qatar
- ▶ Schieffelin JS, Norton EB, Kolls JK. What should define a SARS-CoV-2 "breakthrough" infection? J Clin Invest. 2021 May 11:151186. doi: 10.1172/JCI151186. Epub ahead of print. PMID: 33974565. <https://www.jci.org/articles/view/151186/pdf>

Importance of variants in post-vaccination patients (NEJM 2021)

- ▶ Case report/s with strong laboratory components
- ▶ Rockefeller University follow up study with frequent salivary testing
- ▶ 2 cases, fully vaccinated with Pfizer BNT vaccine, developed signs and symptoms of Covid-19 >2 weeks post second dose
- ▶ Both participants developed moderate symptoms/signs of infection, recovered at home..no CXR reported
- ▶ Both found to have strong antibody response to vaccine, but each had a new variant sequenced that caused infection
- ▶ Transmission risk not able to be assessed