

## CORRESPONDENCE

## Facial Masking for Covid-19

**TO THE EDITOR:** We caution against incorporating hypotheses about masks functioning as effective “variolation” — a notion that was advanced by Gandhi and Rutherford in the *Journal* (online September 8)<sup>1</sup> — into public health messaging without considering the implications and nuances. The term “variolation” should be avoided because it is inaccurate with respect to coronaviruses, and it describes an obsolete and risky practice that was used for the iatrogenic inoculation of smallpox. There is insufficient evidence to support the claim that masks reduce the infectious dose of SARS-CoV-2 and the severity of Covid-19, much less that their use can induce protective immunity. Substantial knowledge gaps must be addressed before claims are made about the efficacy of face masks in reducing morbidity or eliciting immune responses.

Masks are used primarily to reduce SARS-CoV-2 transmission rather than reduce the dose of infectious particles or mitigate the severity of Covid-19. The suggestion that masks offer an alternative to vaccination without evidence that the benefits outweigh the great risks implicitly encourages reckless behavior. With the lack of a vaccine, nonpharmaceutical interventions continue to be the best preventive tools.<sup>2,3</sup> Transparent, contextualized messaging and embracing uncertainty are essential while science moves forward. Currently, there are too many research gaps to conclude that masks offer benefits beyond reducing transmission risk. We should not advocate for these benefits without fully comprehending the risks.

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1. Gandhi M, Rutherford GW. Facial masking for Covid-19 — potential for “variolation” as we await a vaccine. *N Engl J Med*. DOI: 10.1056/NEJMp2026913.

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**TO THE EDITOR:** Gandhi and Rutherford’s theory regarding the potential for variolation by means of facial masking is not consistent with the emerging science of transmission of SARS-CoV-2. This virus does not appear to follow a classic dose–response relationship (i.e., the lower a viral inoculum exposure, the less severe the disease). Experimental infection studies involving healthy adult macaques have shown that severe clinical disease rarely occurs after respiratory infection in SARS-CoV-2, which would be the expected pathophysiological consequence if the dose–response assumption were valid.<sup>1</sup> Viral replication is related to dose, but disease severity is not. The epidemiology indicates that the occurrence of severe Covid-19 is associated with preexisting conditions and other risk factors, such as age, sex, and pregnancy status.<sup>2</sup>

Though not yet shown in experimental models, the infectious dose of SARS-CoV-2 is probably similar to that of SARS-CoV — approximately 300 virions.<sup>3</sup> Regardless of disease severity, people have high viral titers and infectious virus for at least 8 days after symptom onset. Normal talking can generate up to 3000 1-micron particles per minute in exhaled breath,<sup>4</sup> and each particle could contain more than 250 virions, which means that a single minute of speaking potentially generates more than 750,000 virions. Cloth face coverings have highly variable efficacy depending on both filtering capacity and fit. Wearing a cloth face covering while being near

an infected person for several minutes may not prevent the receipt of an infectious dose, which, as noted above, does not correlate with milder disease.

Finally, the now predominant spike mutation D614G, identified commonly in new Covid-19 cases and emergent over the past 6 months, increases human-to-human transmissibility by improving the efficiency of viral replication without increasing the severity of disease.<sup>5</sup> Cloth face coverings have no specified performance criteria and are in no way equivalent to vaccines, for which efficacy and safety must be shown before they can be widely distributed. Cloth face coverings may be useful in lowering the number of infectious particles emitted by the wearer, but masks should not be solely relied on to lower a wearer's risk of inhaling an infectious dose of SARS-CoV-2 that could result in serious and potentially life-threatening disease outcomes.

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2. CDC updates, expands list of people at risk of severe COVID-19 illness. Press release from the Centers for Disease Control and Prevention. June 25, 2020 (<https://www.cdc.gov/media/releases/2020/p0625-update-expands-covid-19.html>).
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**THE AUTHORS REPLY:** We agree that well-described host characteristics, including age and coexisting conditions, influence disease severity. How-

ever, more evidence is accruing to support the idea that the viral inoculum of SARS-CoV-2 (lowered by means of masking or social distancing) is associated with disease severity.<sup>1-4</sup> Direct experimentation in humans to support this theory is not feasible, but studies in animals have shown the association; in addition to the hamster model, which we cited in our Perspective article, a new model in ferrets shows the same dose-response relationship.<sup>3</sup> The association between viral inoculum and disease severity may be related to an overwhelmed innate immune response and has been seen in other viral infections in which the host immune response contributes prominently to viral pathogenesis, such as in SARS-CoV-2, measles, influenza, and dengue.

The use of the term “variation” refers to the fact that strong T-cell immunity to SARS-CoV-2 appears to be generated with asymptomatic or mild infection, as shown in multiple recent studies; the duration of that immunity is unknown, and we stress the need for a safe and effective vaccine. We did not mean to imply in our Perspective article that people should be deliberately infected with SARS-CoV-2. In fact, as practicing infectious disease physicians, we counsel very strongly against deliberate infection, given the case fatality rate and the complicated interplay between host and pathogen. However, because vaccine trials are also examining strategies for reducing the severity of infection, we are interested in any public health strategy (including masking or social distancing<sup>4</sup>) that could reduce disease severity.

Although the evidence regarding reduced transmission and acquisition of infection with the wearing of cloth masks was originally mixed, there is increasing evidence both from physical sciences and from epidemiologic investigations that cloth masks (if worn properly) reduce both transmission and acquisition.<sup>5</sup> The data have evolved on cloth and surgical masks, leading the state of California, for instance, to change its public health messaging to “masks protect you and others.” We hope our article encourages investigators to conduct further studies of the relationship between viral inoculum and disease severity with SARS-CoV-2. Although proving this hypothesis by means of experiments in humans will never be feasible, further studies in animals and observational studies will strengthen the evidence base.

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Since publication of their article, the authors report no further potential conflict of interest.

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