Open Access Journal [doi: 10.46683/jmvi.2020.9] Editorial / Editoryal

Journal of Molecular Virology and Immunology

Can Facial Masking Slow Down the Spread of SARS-CoV-2 by a Variolation-like Effect?

Maske Kullanımı Variyolasyon Benzeri Bir Etki ile SARS-CoV-2 Yayılımını Yavaşlatabilir mi?

Fatih ŞAHİNER[1] [ID]

[1]Department of Medical Microbiology, Gulhane Medical Faculty, University of Health Sciences, Ankara, Turkey.

Article Info: Published in Journal of Molecular Virology and Immunology, 18.09.2020.
Correspondence: Fatih Şahiner; Assoc.Prof., Department of Medical Microbiology, Gulhane Medical Faculty, University of Health Sciences, Ankara, Turkey. E-mail: fsvirol@gmail.com

Numerous studies have been published providing evidence that the universal use of masks reduces the spread of SARS-CoV-2 infections indoors, in hospitals, and public places. Studies in experimental animal models for SARS-CoV-2 infections have shown that more severe lung abnormalities develop in animals infected with high doses of the virus. From this point of view, even if the use of a mask does not absolutely protect from infection transmission, it can contribute to the mild course of possible infections through low viral load exposure. However, in some published studies, it was revealed that antibodies against the virus decreased more rapidly in people who had the infection asymptomatically. In addition, cases of re-infection with different variants of the virus as soon as several months after recovery from the first infection have recently been reported. Considering that coronaviruses generally cause infections with low protective immunity, until a protective vaccine is developed, continuing to use masks seems to be an effective measure that can reduce social spreading of the infection and give protection from serious infections at the individual level, especially in indoor and crowded environments where the transmission risk is high, including for people recovering from infection. As a result, even if the mask does not retain 100% of viruses, it reduces the risk of severe infection because it reduces the viral load to a large degree. In fact, the expected effect of the eagerly anticipated vaccine is nothing more than this.

Universal maske kullanımının kapalı alanlarda, hastanelerde ve halka açık alanlarda SARS-CoV-2 enfeksiyonlarının yayılımını azalttığına dair kanıtlar içeren çok sayıda araştırma yayımlanmıştır. SARS-CoV-2 enfeksiyonları için deneysel hayvan modellerinde yapılan çalışmalarda ise yüksek doz virüsle enfekte edilen hayvanlarda daha ciddi akciğer anormalliklerinin geliştiği gösterildi. Bu noktadan maske kullanımı enfeksiyon bulaşını mutlak bir şekilde korumasa bile, düşük viral yük maruziyeti ile olası enfeksiyonların hafif geçirilmesine katkıda bulunabilir. Bununla beraber yayımlanan bazı çalışmalarda enfeksiyonu asemptomatik olarak geçiren kişilerde virüse karşı oluşan antikorların daha hızlı düşüş gösterdiği ortaya kondu. Ayrıca, yakın zamanda ilk enfeksiyondan iyileştikten birkaç ay gibi kısa bir süre sonra virüsün farklı varyantları ile enfeksiyona ikinci kez yakalanan olgular bildirildi. Koronavirusların genel olarak düşük koruyucu bağışıklık bırakan enfeksiyonlara neden olduğu dikkate alındığında, koruyucu bir aşı geliştirilinceye kadar; enfeksiyonu geçiren ve iyileşen kişiler de dahil olmak üzere, bulaş riskinin yüksek olduğu kapalı ve kalabalık ortamlar başta olmak üzere, maske kullanımına devam etmek enfeksiyonun toplumsal yayılımını ve bireysel düzeyde de ciddi seyirli enfeksiyonlardan korunmayı sağlayabilecek etkili bir önlem gibi gözüküyor. Sonuç olarak, maske virüs geçişini %100 engellemese bile viral yükü çok azalttığı için ciddi enfeksiyon riskini azaltır. Heyecanla yolu gözlenen aşından beklenen etki de bundan başka bir şey değil aslında.

Facial Masking Protects from Severe Infection

There is a potential relationship between the initial transmission viral load and the risk of developing infection in the course of viral infections [1-3]. Although certain estimates (such as 100 viral particles) have been made for the infectious dose of SARS-CoV-2 based on animal research and modeling studies, no definitive results have yet been demonstrated experimentally in humans due to serious risks [4].

A second concept other than the infectious dose is the relationship between the initial exposure dose and the severity of infection symptoms and clinical signs. The initial exposure dose for influenza infections has been demonstrated in numerous experimental studies on animals, and the results of these studies were discussed in detail in a modeling study on the "Second and Third Wave of 1918–1919 Influenza Pandemic" [5]. Similarly, a recent study revealed that more severe lung abnormalities develop in animals infected with high-dose SARS-CoV-2 in a small animal model (Syrian hamsters) [6]. The Center for Disease Control currently advises even the public to wear cloth masks when outdoors [7]. The universal use of a mask, one of the most important tools of COVID-19 epidemic control after isolation and distancing, can prevent virus transmission or help reduce the severity of the disease by reducing the viral load to the exposed [8,9]. As a result, the use of masks combined with social distancing, careful hand hygiene, and other proven preventive measures can significantly slow the COVID-19 outbreak [10]. However, the expected benefit (variolation-like effect) from infections with low viral load exposure can be problematic, when using a mask, since the immune response becomes limited as the virus load is reduced.

A third issue is the level of immunity (both humoral and cellular aspects) that occurs after previous infections to protect against possible future infections. Recently, the first confirmed SARS-CoV-2 reinfection case was reported, and the predictions that the immune response acquired after SARS-CoV-2 infections was not very strong were confirmed [11]. This person, who was proven to be reinfected with a different virus variant, was asymptomatic when he had the infection a second time and was detected during routine screenings. Interestingly, in another case, secondary infection with a different virus variant resulted in a more severe clinical picture in a person who had mild symptoms when the infection was first exposed [12]. This second case can be interpreted as indicating that asymptomatic infections do not produce strong protective immunity. In a study comparing symptomatic (n = 37) and asymptomatic cases (n = 37), a finding supporting this interpretation was presented, that while immunoglobulin G (IgG) decreased in both symptomatic and asymptomatic patients, 13% of symptomatic patients became seronegative in the eighth week, although this rate was 40% higher in asymptomatic patients [13]. In the same study, it was shown that anti-inflammatory and pro-inflammatory cytokine levels, which are indicators of an immune response, were at lower levels in asymptomatic individuals.

Of course, there are promising results regarding the immune response. In a study, it was reported that seropositivity was detected in 1,107 (91.1%) of 1,215 people who had SARS-CoV-2 infection and recovered, and antiviral antibodies against SARS-CoV-2 did not decline within four months after diagnosis [14]. Although not enough time has passed to assess SARS-CoV-2 infections, SARS-specific antibodies were maintained for an average of two years in people who had recovered from the 2003 SARS epidemic [15]. It should not be forgotten that data have shown that the immune response is not just a humoral response and that cellular immunity plays an important role in SARS-CoV-2 infections [16,17].

But after all, the lack of permanent immunity against seasonal coronaviruses and the inability to develop a successful vaccine for SARS-CoV and MERS-CoV, despite many years of efforts, are other indicators that coronavirus infections do not produce a strong immunity [18].

Variolation and vaccination

Smallpox virus, a member of the Poxviridae family, produces a very strong immune response

both after natural infections and by vaccination [19]. Therefore, with the contribution of this feature and being a virus that only causes infections in humans, it was the first virus and first disease to be eradicated by human efforts and vaccination worldwide in 1979 [20]. Variolation is a technique that was first used in the Far East (China and India) and the Ottoman Empire and later developed in Britain [20]. Variolation consists of administering particles derived "by drying the liquid taken from the vesicles of people with smallpox in the sun" or "scraping off healing crusts" to the noses or skin of susceptible individuals. This practice significantly (20–30% to 1–2%) reduced infection mortality, but still remained a risky practice [19,20]. Afterwards, as the first example of safe vaccination implied by Edward Jenner, safe protection from smallpox infections was provided by inoculating the skin infected with the cowpox virus, which has antigenic properties close to the smallpox virus (Figure 1) [20]. This is due to the fact that the smallpox virus and its closely related viruses have antigenic structures that are well protected, give cross-reactivity, and have the ability to produce a strong immune response maintained 30 years or longer [19,20]. At the same time, in SARS-CoV-2 infections, which are open to the risk of re-infection with variants with very small differences, a very strong immunity does not occur in humans and animals and is maintained only three months to two to three years (estimated) [13-15]. As a matter of fact, it has been announced that a vaccine that protects 50% of susceptible people or reduces disease severity in 50% of patients may be sufficient for a vaccine that is considered for approval by the US Food and Drug Administration (FDA) [21]. Thus, vaccine expectations have been lowered, but even such a vaccine can be very effective in stopping the pandemic. The same holds true for hepatitis C virus (HCV) vaccines, and it has been argued that even a vaccine to reduce chronicity could be beneficial even without a preventive vaccine [22]. For these reasons, instead of keeping the expectations about vaccines very high, the use of these vaccines should be decided by making possible benefits in epidemic management, reducing disease severity, and cost-effectiveness analyses.

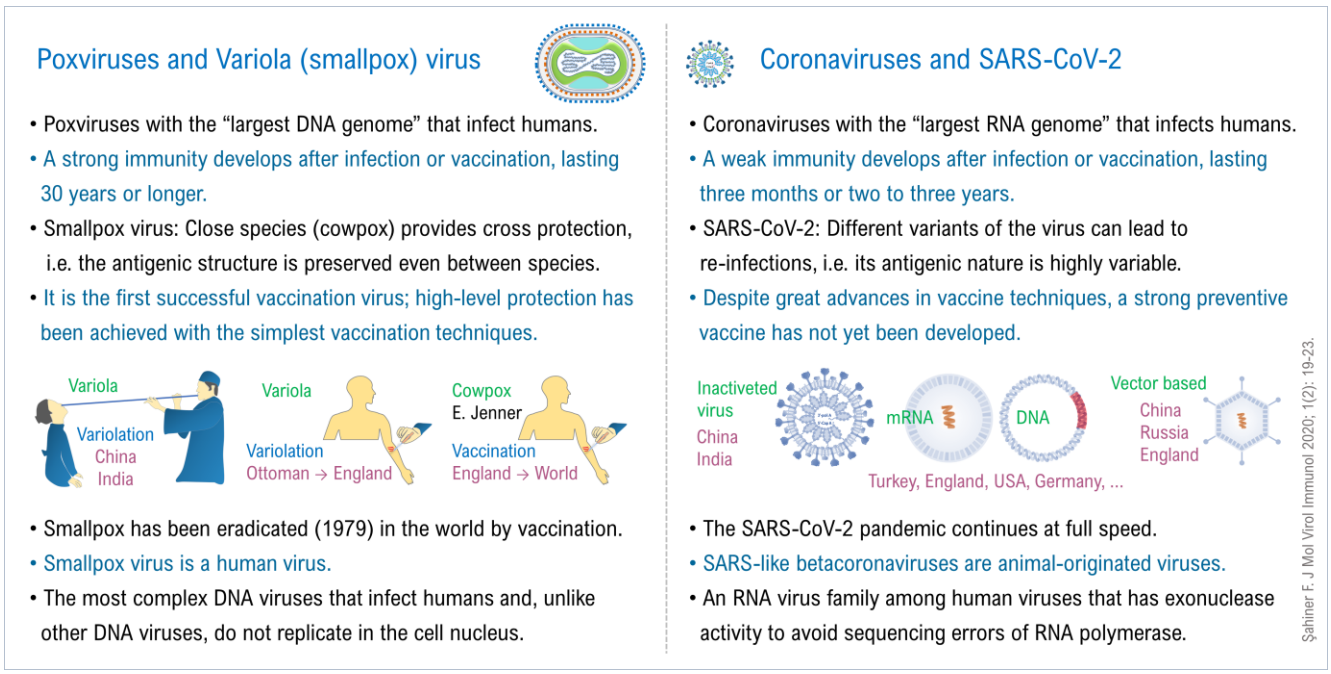

Figure 1. First and most recent examples of vaccine applications; as technology improves, protecting humanity is getting harder and harder.

Contributing to the mild course of infections by reducing the viral load in initial transmission is an important benefit of the use of masks; there is ample evidence to support that wearing masks in hospital settings, other confined spaces, and public spaces will contribute to a reduction in the

spread of infection [8,23]. However, considering the data on the strength and duration of the immune response that develops in coronavirus infections, it appears that even if the use of a mask has a variolation-like effect, it will be at a very low level. Therefore, considering that this low immunity may be insufficient to protect us from future infections, in particular for SARS-CoV-2, it would be a rational approach to continue using masks as if we had never encountered the virus. In addition, since the variolation-like potential benefit of the mask is not a controlled and measurable situation, any misunderstanding on this subject carries certain risks. Still, any suggestion that will contribute to slowing the current epidemic is meaningful and valuable.

At this point, those who have a mild initial infection should not be too complacent and should know that they can be re-infected with different variants of the virus within three months to two years. Also, those who have obvious symptoms when they first have the infection are warned not to take their condition lightly, because it seems possible to have a milder second infection with a different variant of the virus and to spread this new virus to the environment without realizing it. Until an effective vaccine is available, everyone should continue to wear a mask, including those who have never been sick, those who have recently recovered, or those who have had the disease without symptoms.

Conflict of interest: The author declares that there is no conflict of interest. The author alone is responsible for the content and writing of the paper.

Financial disclosure: There is no financial support to this study.

References

1. Yazdanpanah Y, De Carli G, Migueres B, Lot F, Campins M, Colombo C, et al. Risk factors for hepatitis C virus transmission to health care workers after occupational exposure: a European case-control study. Clin Infect Dis 2005; 41(10): 1423-30. [Crossref]

2. Dietrich U. Advances in Antibody-Based HIV-1 Vaccines Development. Vaccines (Basel). 2020; 8(1): 44. [Crossref]

3. Yezli S, Otter JA. Minimum Infective Dose of the Major Human Respiratory and Enteric Viruses Transmitted Through Food and the Environment. Food Environ Virol 2011; 3(1): 1-30. [Crossref]

4. Karimzadeh S, Bhopal R, Nguyen Tien H. Review of Infective Dose, Routes of Transmission, and Outcome of COVID-19 Caused by the SARS-CoV-2 Virus: Comparison with Other Respiratory Viruses. Preprints 2020; 2020070613.

5. Paulo AC, Correia-Neves M, Domingos T, Murta AG, Pedrosa J. Influenza infectious dose may explain the high mortality of the second and third wave of 1918-1919 influenza pandemic. PLoS One 2010; 5(7): e11655. [Crossref]

6. Imai M, Iwatsuki-Horimoto K, Hatta M, Loeber S, Halfmann PJ, Nakajima N, et al. Syrian hamsters as a small animal model for SARS-CoV-2 infection and countermeasure development. Proc Natl Acad Sci U S A 2020; 117(28): 16587-95. [Crossref]

7. Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, USA. Recommendation Regarding the Use of Cloth Face Coverings. 3 April 2020. Available at: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/cloth-facecover.html [Accessed April 9, 2020].

8. Gandhi M, Rutherford GW. Facial Masking for Covid-19 - Potential for "Variolation" as We Await a Vaccine. N Engl J Med 2020; 10.1056/NEJMp2026913. [Crossref]

9. Střížová Z, Bartůňková J, Smrž D. Can wearing face masks in public affect transmission route and viral load in COVID-19?. Cent Eur J Public Health 2020; 28(2): 161-2. [Crossref]

10. Tirupathi R, Bharathidasan K, Palabindala V, Salim SA, Al-Tawfiq JA. Comprehensive review of mask utility and challenges during the COVID-19 pandemic. Infez Med 2020; 28(suppl 1): 57-63.

11. To KK, Hung IF, Ip JD, Chu AW, Chan WM, et al. COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. Clin Infect Dis 2020; ciaa1275. [Crossref]

12. Tillett R, Sevinsky J, Hartley P, Kerwin H, Crawford N, Gorzalski A, et al. Genomic Evidence for a Case of Reinfection with SARS-CoV-2. SSRN 2020; 3680955. [Crossref]

13. Long QX, Tang XJ, Shi QL, Li Q, Deng HJ, Yuan J, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. Nat Med 2020; 26(8): 1200-4. [Crossref]

14. Gudbjartsson DF, Norddahl GL, Melsted P, Gunnarsdottir K, Holm H, Eythorsson E, et al. Humoral Immune Response to SARS-CoV-2 in Iceland. N Engl J Med 2020; 10.1056/NEJMoa2026116. [published online ahead of print] [Crossref]

15. Wu LP, Wang NC, Chang YH, Tian XY, Na DY, Zhang LY, et al. Duration of antibody responses after severe acute respiratory syndrome. Emerg Infect Dis 2007; 13(10): 1562-4. [Crossref]

16. Chen Z, John Wherry E. T cell responses in patients with COVID-19. Nat Rev Immunol 2020; 20(9): 529-36. [Crossref]

17. Ozcelik F, Tanoglu A, Çıracı MZ, Ozcelik IK. Use of Immune Modulator Interferon-Gamma to Support Combating COVID-19 Pandemic. International Journal of Coronaviruses 2020; 1(1): 1-15. [Crossref]

18. Sariol A, Perlman S. Lessons for COVID-19 Immunity from Other Coronavirus Infections. Immunity 2020; 53(2): 248-63. [Crossref]

19. Cohen J. Bioterrorism. Smallpox vaccinations: how much protection remains?. Science 2001; 294(5544): 985. [Crossref]

20. Behbehani AM. The smallpox story: life and death of an old disease. Microbiol Rev 1983; 47(4): 455-509.

21. US Food and Drug Administration (FDA), Silver Spring, Maryland, USA. Coronavirus (COVID-19) Update: FDA Takes Action to Help Facilitate Timely Development of Safe, Effective COVID-19 Vaccines. Available at: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-takes-action-help-facilitate-timely-development-safe-effective-covid [Accessed August 29, 2020].

22. Bailey JR, Barnes E, Cox AL. Approaches, Progress, and Challenges to Hepatitis C Vaccine Development. Gastroenterology 2019; 156(2): 418-30. [Crossref]

23. Wang X, Ferro EG, Zhou G, Hashimoto D, Bhatt DL. Association Between Universal Masking in a Health Care System and SARS-CoV-2 Positivity Among Health Care Workers. JAMA 2020; 324(7): 703-4. [Crossref]