

# Facial Masking and SAMPPs: Potential “Variolation” in COVID-19

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Variolation is an important phenomenon in the field of immunology and has a rich historical background that has changed the perception of immunity reinforcement in human beings.<sup>1</sup> This methodology was first used to immunize humans against smallpox infection by inoculating the infective material taken from infected patients.<sup>2</sup> The intention was to induce a mild form of infection that would generate antibody response for tackling the future smallpox infection. To be more precise the procedure involves the application of powdered smallpox scabs or fluid obtained from the pustules of the infected patients. This application is on the superficial scratches made on the skin surface of normal healthy individuals.<sup>3</sup> Thus, the variolation is the process in which the virus is inoculated in the patient to produce an antibody response. This process produces signs and symptoms similar to the intended viral infection but usually of the milder form, possibly due to mild quantum exposure of virus particles. In the case of smallpox, this methodology was first used in China, India, and the Middle East before it was introduced into England and North America in the 1720s.<sup>4</sup> Due to advancements done in the field of vaccination, this crude method is no longer used today. However, this process was a milestone in science that has led to the development of many vaccines available nowadays.

For almost a year now, novel coronavirus-disease (COVID-19) has been spreading all over the world causing significant morbidity and mortality.<sup>5</sup> High degree of infectivity is the main reason for all the consequences which is mainly attributed to the SPIKE receptors of the virus and its binding to abundant ACE2 protein on the human.<sup>6</sup> In this difficult scenario, the only hope for tackling this deadly infection is the massive vaccination drive across the globe. This process has already taken place in many countries with emergency approval from guiding authorities and bodies. Unfortunately, the developed RNA-based vaccination would suffer from recently reported mutations in the virus.<sup>7</sup> Hence, considering the possibility of variolation in COVID-19 infection would be a good proposition and there is a dire need for investigation in this direction.

With this view in mind, we have made efforts to find out the literature for possible variolation phenomenon in COVID-19. The first evidence of a possible effect of variolation in COVID-19 was proposed by Sharma et al.<sup>8</sup> They proposed the working of natural vaccines in the form of SARS-CoV-2 associated molecular particle patterns (SAMPPs) that can be generated on the inanimate surfaces, facemasks, and other potential surroundings during sanitization by alcohol and detergents. It was envisaged that SARS-CoV-2 biological components, such as RNA, lipid, and proteins including SPIKE-2 glycoproteins form the composition for SAMPPs and can

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potentially generate adaptive immunity once they come in contact with antigen-presenting cells associated with mucosa. In a similar context, Gandhi et al.<sup>9</sup> proposed the scientific explanations by hypothesizing the impact of universal face masking that may be linked with the potential variolation among the exposed human population and generation of adaptive immunity. We looked at these effects with regards to the recent rise in the asymptomatic cases and also the significant low mortality rate. Moreover, recent studies on seroprevalence, which suggest a large portion of the population with antibodies against the COVID-19 virus, also support the proposition of possible variolation.

We are intrigued by these two proposals and recommend that the recent rise in asymptomatic/presymptomatic cases and a decrease in mortality rate should be discussed in the larger perspectives of facial masking and SAMPPs related to variolation. Altogether, the COVID-19 vaccine at the natural level is reinforced by taking into consideration of perspectives suggested by both Gandhi et al. and Sharma et al., in timely importance to preclinical, clinical, and society at large. This proposition will not only have implications for the healthcare sector but also help in improving the economic stability of the nations.

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