

Immunity and protection from COVID-19—Environmental mycobacteria play a role

To the Editor,

Kerboua et al¹ discussed about the immunity induced by nonspecific inflammation and Bacillus Calmette-Guerin (BCG) as factors altering the susceptibility to severe illness from coronavirus disease 2019 (COVID-19). Ozdemir et al² in their study have shown proportionately less number of cases, milder illness and a lower death rate in BCG vaccinated population as compared with BCG non-vaccinated across different countries and hemispheres.² But BCG vaccination in childhood does not have prolonged protective effect against tuberculosis (TB) in adulthood as the effect of BCG vaccination is moderate and lasts for nearly up to 15 years.³ Therefore the protective effect may not be applicable to COVID-19 beyond some years since vaccination, particularly during adulthood. As there is some degree of protection as discussed^{1,2} and the protections are nonspecific, there might be some other factors decreasing the virulence and pathogenicity of COVID-19 beyond the protection duration of BCG.

BCG vaccination has a protective effect on viral infection in humans. Such effects are believed to be mediated by heterologous lymphocyte activation and the initiation of innate immune memory. As a result, there are enhanced cytokine production, macrophage activity, and increased interferon- γ production from CD4⁺ lymphocytes.⁴ Severity of the COVID-19 depends on the level of cytokine storm and T cell lymphopenia and both are associated with pulmonary damage, respiratory distress and higher mortality. BCG also induces epigenetic and functional reprogramming in human mononuclear cells and increases the level of immunity for unrelated viral infections and interleukin-1 β plays as mediator of trained immunity responses.⁴

In a study in south India the immune responses of nonvaccinated tuberculin reactors in India have shown to have significantly higher than the vaccinated tuberculin non-reactors.^{5,6} Nonvaccinated person also develop natural immunity with the time through the repeated exposure with ubiquitous environmental mycobacteria.⁷


In the TB endemic countries like India with high population density, the environmental mycobacteria seems to play a role as over half of the population are usually positive for tuberculin skin test (TST). Factually these conditions impact some degree of general immunity for new infections. The development of nonspecific (off-target) partial immunity is likely from environmental mycobacteria as people from TB endemic countries like India get infected from the environment time to time. Possibly it is one of the reasons most of the people become TST positive.⁶

It is a plausible hypothesis that environmental mycobacteria like non-tuberculous mycobacteria (NTM) are imparting similar to BCG but sustained nonspecific immunological response that may be correlated

with reduced disease burden and severity of COVID-19. The ubiquitous persistence of NTM contributes to impart immune responses, whose effect is measured by positive TST particularly in BCG-nonvaccinated population. It is also hypothesized that environmental mycobacteria induce repeated alteration in the immune system resulting increased level of innate and adaptive or trained immunity. The environmental mycobacteria might have induced trained immunity making epigenetic alterations in the similar mechanism as described for BCG.⁷ It is likely that the environmental mycobacteria play a role beyond the protection of BCG and more importantly for nonvaccinated people. This hypothesis can support the concept of partial protection from COVID-19 in countries where BCG vaccination is not routine. However further study is needed to confirm the hypothesis.

In fact, repeated exposure to environmental mycobacteria is presumed to be the explanation for the low efficacy of BCG vaccination particularly in tropical regions. Furthermore, because of cross-reactivity among mycobacterial species, exposure to environmental mycobacteria may provide some protection against TB, and also it can induce positive TST.⁸ TB endemicity or environmental mycobacteria seems to be correlated with reduced disease burden and severity of COVID-19.

It is possible that people of the TB endemic countries like India despite vast population and growing numbers of COVID-19 infection, have acquired some protections from severity and deaths from COVID-19 in comparison to TB non-endemic countries (like Europe and USA). Although it appears that such nonspecific immunity may not be able to stop COVID-19 infections, but is likely to diminish its impact on severity of COVID-19.

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