

Current Speculations on the Low Incidence Rate of the COVID-19 among Children

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Dear Editor

First reported in Wuhan, China on December 2019, the coronavirus disease 2019 (COVID-19) is a contagious viral infection of the respiratory system caused by SARS-CoV-2 (1). As of April 26, 2020, more than 2.5 million people have contracted the disease with nearly 200,000 deaths (2). The data published on the mortality and morbidity of the disease suggest that children under 10 years of age are generally less vulnerable to the virus and are usually asymptomatic or show milder symptoms (3). On the other hand, adults and the elderly, particularly those with underlying health conditions, appear to be more susceptible to the disease (4). It is not clear why children are more immune to COVID-19. However, we have an idea which we would like to share with the general public and scientific communities, hoping this would hinder the further spread of the disease.

Children are routinely vaccinated against a number of bacterial and viral diseases, including tuberculosis, diphtheria, pertussis, measles, rubella, mumps, hepatitis A, and hepatitis B. We initially thought that these bacteria and viruses might have the same antigenic structure as the spike (S) protein and nucleocapsid (N) protein of SARS-CoV-2. It is known that the spike (S) protein plays a key role in the binding of viruses to a specific receptor on the epithelial cells of the respiratory system. In addition, both spike (S) and nucleocapsid (N) proteins are the main immunogenic proteins of SARS-CoV-2 that induce the host immune system (5). Therefore, neutralization of the antibodies produced against the foregoing vaccine-preventable microbes might cross-react with the antigenic epitopes of the spike (S) and nucleocapsid (N) proteins and

prevent COVID-19 in children.

To investigate this hypothesis, using the BLAST search tool, we conducted a sequence homology search for the Spike (S) and nucleocapsid (N) proteins of SARS-CoV-2 against the proteomic database of the aforementioned vaccine-preventable microorganisms. The results showed no significant sequence similarity between these proteins and those in the childhood vaccine-preventable microbes. This suggests that memory T-cells, rather than vaccine neutralizing antibodies, may be involved in the protection of children against COVID-19. This is because children have a larger number of naive T-cells that can be programmed to protect them against the disease (6). This is consistent with a study in which the levels of SARS-CoV-2 specific antibodies correlated with age among 175 COVID-19 recovered patients. Elderly and middle-aged subjects developed higher levels of antibodies and lower blood lymphocyte counts compared to the younger patients. Meanwhile, no SARS-CoV-2 specific antibodies were detected in 6% of those younger than 40 (7). Our proposal can be further supported by the fact that children uniquely own active thymus, a lymphatic organ in which the formed T-cells mature, develop, and reproduce to fight the intracellular pathogens throughout childhood (8).

There are other hypotheses proposed to elucidate the immunity of children against COVID-19. For instance, Brodin P (2020) suggested that other viruses in the respiratory system of children could offer protection against SARS-CoV-2 through virus-to-virus interaction and competition (3). Additionally, it is feasible to generate a broad humoral immunity against the viruses, particularly when the whole viral particle

is introduced to the immune system, as is the case with measles or rubella vaccination (9). There is a report on a cross-protection immune response against the lethal 1918 Spanish influenza A virus through 2009 H1N1 influenza virus vaccine (10). The antibodies produced against one or more of the vaccine-preventable diseases may further protect children against COVID-19.

In summary, children are generally less vulnerable to COVID-19. We hypothesized that the immunity created via routine childhood immunization might reduce the morbidity rate of COVID-19 among children. Our result suggested that the cellular immunity (memory T-cells) might contribute to the children's protection to this virus.

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