

COVID-19 herd immunity by immunisation: are children in the herd?



The scourge of COVID-19 has been global, but the most affected subgroups in the population have largely been older people and individuals with comorbid conditions that predispose them to increasingly severe disease and poor outcomes. Overall, the disease burden in children has been reasonably mild, even in those with comorbidities, such as oncological conditions. Protection from severe disease in children might be related to a lower expression of host factors required for viral replication, and to differences in the magnitude and timing of innate or adaptive immune responses. Data for recorded COVID-19 cases show that only 7% of children younger than 18 years with severe disease required intensive care, whereas 53% of adults who had severe disease required intensive care.¹⁻³ Multisystem inflammatory syndrome in children, arguably the most dreaded presentation, typically presents between 3 and 6 weeks after SARS-CoV-2 exposure.⁴ Most patients at presentation have a negative nasopharyngeal RT-PCR but are positive for serology. This temporal association and low PCR positivity rate suggest a postinfectious mechanism rather than acute viral infection. Children of African or Hispanic race or ethnicity are more frequently affected, whereas children of Asian or White race or ethnicity appear to be less often affected,^{5,6} and genetic susceptibility might account for this over-representation. The reasonably low incidence of COVID-19 in the general population of children, the unusual manifestation with multisystem inflammatory syndrome in older children and adolescents, and the absence of epidemiological data that incriminates children in the transmission of SARS-CoV-2, pose important immunological, ethical, and economic conundrums that require careful examination before the deployment of any COVID-19 vaccine in children.

The following clinical observations are relevant for formulating COVID-19 vaccines for deployment in children.

First, from an immunological perspective, the milder spectrum of disease in children might correlate with SARS-CoV-2 antigen processing and immunopathogenesis in children. Few immunological studies in children with multisystem inflammatory syndrome report abnormal

immunophenotypes of plasmablasts,^{7,8} elevated SARS-CoV-2 IgG, and proinflammatory cytokines.⁸ Current vaccines that are authorised for emergency use, approved or in development, do not have a safety or immunogenicity profile in children. In the absence of a better understanding of the pathogenesis of this condition, using the same approach for delivering vaccines as in adults could exacerbate the incidence of this hyperinflammatory condition.

Second, from a public health perspective, it will be necessary to immunise children if they are a major source of SARS-CoV-2 transmission and if the candidate vaccines block transmission. However, epidemiological reports up to now suggest that young children have a high likelihood of developing COVID-19 via household transmission, once a family member tests positive for COVID-19.¹ There is little evidence of secondary infection from children to others in the transmission pathways of COVID-19. Although emerging data suggest that some candidate vaccines can block transmission, vaccinating children cannot be justified if it is to give direct protection despite minimal burden of disease or to help to block transmission if children do not constitute a substantial reservoir for transmission. For other infections that can be prevented by vaccine, such as invasive pneumococcal disease, immunisation of children not only prevented infections in children, but also conferred indirect benefit by decreasing disease in older people, because of its effect on carriage reduction and blockage of transmission.⁹ For COVID-19, the reverse might be the case, with adults having to be vaccinated to confer protection on young children.

Third, from an ethical perspective, there is a balance between risk and benefit in offering a COVID-19 vaccine to children that will offer minimal or no direct benefit to the recipient, no benefit to the public, and as yet, unknown medium-term and long-term risks to the recipient. Other important considerations include the economic and practical considerations in deploying a new vaccine into the routine childhood immunisation programmes. Without additional data and public enlightenment on the benefits of immunising young children, this deployment

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could further threaten childhood immunisation coverage that is already precariously low in several settings.

Finally, because individuals are not equally susceptible and contagious, our current target to vaccinate 65–70% of the population to archive herd immunity might be an overestimate.¹⁰ If young children are excluded, there will be more vaccines available for the more epidemiologically susceptible subgroups. Initiating efficacy trials in youths aged 12–18 years is a welcome development, but a new strategy might ultimately be required for immunising younger children, should this become necessary.

I declare no competing interests.

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