

Therapeutic Advances in Vaccines and Immunotherapy

Letter to the Editor

COVID-19: should oral vaccination strategies be given more consideration?

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mucosal route may allow more potent induction of humoral (antibody-mediated) and cellular immune responses, priming the body to respond effectively to respiratory challenges.⁶ In addition, as documented with the oral polio and rotavirus vaccines, the possibility of faecal shedding of oral vaccines may accelerate herd immunity through oro-faecal transmission in close contacts, particularly in the developing world.^{7,8}

Oral vaccines may also be manufactured more simply, highlighting the scalability of this approach.2 The ease of oral inoculation also removes the requirement for trained healthcare professionals to be present to administer the vaccine, minimising cross-infection risk at healthcare centres, whilst potentially maximising uptake and compliance. This may significantly expand practical options for vaccine distribution, particularly in resource-limited settings that are worst affected, given that other preventive measures, such as social distancing, may be harder to implement.9 In addition, thermally stable oral formulations in the past have been independent of a temperature-controlled supply chain, potentially further simplifying distribution logistics by eliminating a significant contributor of cost in vaccine distribution programmes.¹⁰ It is possible that oral vaccines may be effective as a complementary approach, preferentially employed in resource-limited, population-dense settings.

Taken together, the development of a successful oral formulation may offer relative advantages concerning safety, efficacy, compliance, ease of manufacturing and administration. These factors are essential to consider when developing globally scalable immunisation strategies against SARS-CoV-2.

The novel coronavirus, SARS-CoV-2, has led to an unprecedented international health crisis. The implementation of a vaccine is essential to accelerate herd immunity, enabling lockdown measures to be relaxed and socioeconomic activity to safely resume whilst limiting the case fatality rate. A concerted global effort has led to over 150 vaccines currently under development. However, it is apparent that oral administration has been markedly under addressed as a potentially effective immunological strategy.

Research has now revealed a high expression of the SARS-CoV-2 receptor, ACE2, and the serine protease for virus spike protein priming, TMPRSS2, in absorptive enterocytes of the ileum and colon.1 This highlights a non-canonical route of host invasion for SARS-CoV-2, and a potential site at which artificial immune induction through an oral vaccine could be protective.

Oral immunisation is a viable strategy that has been implemented successfully in preventing respiratory illness.² For example, the live oral enteric-coated adenovirus type 4 and type 7 vaccines, approved for use in US military personnel 17-50 years of age, have been shown to be safe and highly effective in reducing disease burden in numerous clinical trials.3 These vaccines cause an asymptomatic infection of the gut and subsequently generate mucosal immunity to protect against future respiratory illness.4 More recently, an orally administered influenza vaccine has progressed successfully through phase II clinical trials, highlighting the promising potential and ongoing active development of oral vaccines for respiratory disease.5

Several benefits may be attained through employing an oral approach. Evidence suggests that the Therapeutic Advances in Vaccines and Immunotherapy

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Conflict of interest statement

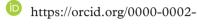
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