DOI: 10.1002/rmv.2303

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EDITORIAL

Protection offered by SARS coronavirus 2 vaccines against disease and infection

At the time of writing, Israel is experiencing a new wave of SARS coronavirus 2 (SARS-CoV-2) infection and Covid-19 disease despite having a high vaccine uptake with both doses of Pfizer/BioNTech mRNA vaccine. This has prompted UK politicians to propose a booster dose for adults in this country. It may therefore be timely to remind them about what we have learned over the years about the principles of vaccinology in order to inform their decisions more effectively.

Successful vaccines prevent disease.[1] They may also prevent transmission of virus between individuals depending on the characteristics of the vaccine used. For example, killed poliovirus vaccine effectively prevents disease by providing IgG antibodies that block the ability of poliovirus in the gastrointestinal tract to use the bloodstream to reach the anterior horn cells of the spinal cord. Live, attenuated poliovirus vaccine likewise provides these IgG antibodies to protect against disease but also induces secretory IgA antibodies in the gastrointestinal and respiratory tracts. This local immunity is responsible for reducing transmission of virus from person to person so allowing oral polio vaccine, unlike its killed alternative, to interrupt transmission of virus in the community. This was illustrated clearly in the late 1980s when an outbreak in Israel of wild poliovirus infection was controlled only once oral vaccine was added to the routine schedule of killed vaccine.[2]

The licensed SARS-CoV-2 vaccines based on mRNA and recombinant adenovirus technologies are remarkably potent at preventing Covid-19, especially the deaths that result from overactivity of the immune system.[3] However, in terms of interrupting transmission of SARS-CoV-2, they are behaving more like killed polio vaccine than the live attenuated version. They have some useful activity (perhaps 60%) against transmission of virus, but the consequences of this for vaccine effectiveness in a community need to be related to the strains of SARS-CoV-2 currently circulating. The original strain had a basic reproductive number of around 2.5, meaning that a vaccine that reduced community transmission by 60% would induce herd immunity. However, the emergence of other strains, particularly Delta, has provided viruses with a basic reproductive number of approximately 5 that would require 90% reduction in transmission in order to achieve herd immunity.[4] This explains why Delta infection has continued to circulate in Israel despite a very high uptake of vaccine. Just as SARS-CoV-2 can reinfect after natural infection,[5] it can reinfect after vaccine-induced immunity, especially if individuals do not heed advice about social distancing and so transmit relatively large inocula of virus. Importantly, this phenomenon of transmission within a highly immunised population is directly attributable to the concept of herd immunity and has nothing to do with strains of virus that evade vaccine induced immunity.[6] It can thus be seen that giving booster doses of the original vaccines, or those designed to confer protective immunity against the variants that have genetic changes in the Spike gene, will not be an appropriate way forward. So, what should be done instead?

Applying the poliovirus concept to SARS-CoV-2 suggests that efficient induction of IgG antibodies may be very effective against disease but require alternative ways of inducing secretory antibodies. A search on Pubmed for 'secretory IgA AND Covid-19 vaccines' revealed only two publications, both dealing with IgA in breast milk.[7,8] Clearly, more work is needed on secretory IgA antibodies against SARS-CoV-2 in the respiratory tract. Vaccine developers should examine whether any of the now many types of vaccine currently in development produce high levels of secretory IgA antibodies. Those that do, could be tested in individuals already immunised with licensed vaccines. The example of poliovirus is again instructive here, with both killed and live vaccines currently used in immunisation schedules.[2] At least two novel approaches should also be considered. The first is to develop and deploy live attenuated vaccines. If given as a booster to those already immunised with vaccines based on mRNA or recombinant adenovirus platforms, the precedent of varicella-zoster virus vaccine must then be remembered. The shingles vaccine requires a high dose of virus (approximately 13 times more plaque forming units) of the same strain of live attenuated vaccine given to prevent chickenpox in seronegatives in order to overcome pre-existing antibody levels in those with prior natural chickenpox.[9] The second is to develop a non-replicating vaccine to be given intranasally, or perhaps orally, to stimulate mucosal IgA antibodies.

It is clear that the objective of controlling the spread of SARS-CoV-2 will be a long haul endeavour that will be aided by learning from past examples of successful vaccinology. The rapid development of the currently licensed vaccines has been a major achievement in terms of preventing disease and death, but the answer to the distinct problem of transmission of virus is not necessarily more of the same. I personally see no reason for doses of the current vaccines to be given routinely in the UK to people with normal immunity. Instead, they should be donated to Covax for deployment in other countries

because, as stated eloquently elsewhere, no-one will be safe until everyone is safe.[10]

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