

The Executive Summary has been replaced with a weekly compendium of items relating to immunity and vaccine development

INTERNATIONAL SOS WEEKLY SCIENTIFIC UPDATE Focussing on immunity and vaccine development

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OXFORD VACCINE TRIALS RESUME

The Phase 3 trials of the Oxford AstraZeneca COVID-19 vaccine are to resume. The trials, being held in the UK, Brazil, South Africa and the US, had been halted after a volunteer fell ill.

[AstraZeneca has said](#), "We cannot disclose medical information about the illness for reasons of participant confidentiality. We are committed to the safety of our participants and the highest standards of conduct in our studies and will continue to monitor safety closely."

UNITED ARAB EMIRATES GRANTS EMERGENCY APPROVAL FOR SINOPHARM VACCINE

The United Arab Emirates (UAE) has granted [emergency approval](#) for an inactivated coronavirus vaccine developed in China to be provided to healthcare workers.

The approval came six weeks after Phase 3 testing of the vaccine began in the UAE and which has not been completed. The vaccine had been tested on 31,000 volunteers and had reported only mild and expected side-effects.

The vaccine passed Phase 1 & 2 trials in the UAE with 100% of volunteers generating antibodies after two doses 28 days apart. The trials were jointly operated by G42 Healthcare, a local AI company, and Chinese company Sinopharm. Phase 3 trials of the vaccine are also underway in Peru and Morocco.

Note that Sinopharm have two inactivated virus vaccines in development and that these are different to the "Sinovac" vaccine being developed by Chinese company "Sinovac Biotech".

[From Wikipedia](#): In the USA, consideration of a drug for an Emergency Use Authorization (EUA) requires a finding that it is "reasonable to believe" that the drug "may be effective" "to prevent, diagnose, or treat serious or life-threatening diseases or conditions that can be caused by a [chemical, biological, radiological, and nuclear] agent(s)".

WILL WE NEED A BOOSTER SHOT?

In an excellent article from the [Doherty Institute](#), Nobel Laureate Professor Peter Doherty describes that a booster shot may be “a good idea” with any of the COVID vaccines, or indeed after having been infected with SARS-CoV-2.

He cites the case of the 33 yo man from Hong Kong who has recently been proven to have been infected twice with SARS-CoV-2. This patient was quite symptomatic with his first infection, whereas the second infection was asymptomatic. It is thought that the patient’s immunity had waned sufficiently to allow him to be reinfected.

“The idea that mild reinfection will provide a natural ‘booster shot’ that leads to better, long-term immunity is, in fact, very familiar.” Prof Doherty says.

Prof Doherty describes how the “one-shot” strategy was used when the measles vaccine was first introduced in 1968, however there were outbreaks in the USA by 1981.

“It turned out that children maintained their immunity while there was still enough measles virus circulating in the community to give them a mild reinfection.” he wrote. “The problem was overcome by giving a measles booster.”

THE CONCEPT OF “PRIME-BOOSTING”

Prime-boosting is the concept of using **different** vaccines sequentially to deliver the same antigen to elicit a maximum T-cell memory (cellular immune) response.

An article in “[Trends in Immunology](#)” reviews the topic. It notes that while there have been many vaccine successes, there are other diseases such as HIV, TB and malaria which “resist the humoral (antibody-based) immunity that is characteristically generated by traditional vaccines.”

“Over the past few years, significant effort has been directed to promote potent cellular immunity to these pathogens. One effective technique is the ‘prime-boost’ strategy which involves priming the immune system to a target antigen delivered by one vector and then re-administering the antigen using a different vector.”

The logic behind prime-boosting is that the subject develops **some immunity to the first vector** and this inhibits “robust antigen presentation” when the same vaccine is used to boost.

An example in the context of COVID vaccination may be giving the Oxford vaccine, which uses an adenovirus to deliver the spike antigen, and then boost possibly with a molecular clamp vaccine, such as the one being developed by the University of Queensland.

SUMMARY OF COVID IMMUNITY AND IMPLICATIONS FOR VACCINE

Professor Robert Booy, Professor of Paediatrics and Epidemiologist, University of Sydney, Australia.

[Play HealthEd Podcast](#)

It is important to distinguish a vaccine's "Immunogenicity" from its "Efficacy".

Immunogenicity

- The vaccine stimulates the production of antibodies and maybe a T-cell response
- This may or may not be protective against disease

Efficacy

- Only comes from Phase 3 studies in tens of thousands of people and indicates if the vaccine prevents disease
- The prevention can be 90-100% or only 50-60% depending on how effective the vaccine proves to be

The Oxford/AstraZeneca vaccine is looking hopeful; however, it is not yet confirmed to be protective and safe. We are awaiting the results of the Phase 3 trials, ongoing in Brazil, USA, UK, South Africa and India, which should start becoming available in October and November.

Once a vaccine is released to the market, intensive post-marketing surveillance occurs looking for side-effects that were not identified in the Phase 3 trials. These could be very rare and may only be found when the vaccine is given to hundreds of thousands of people.

When the initial series requires two doses, Prof Booy recommends that the same vaccine be used.

[Note our previous discussion about "prime/boosting" was about booster dose, not the initial series]

At the moment it is unclear if the initial series of the Oxford/AstraZeneca vaccine will require one or two doses:

- The Phase 3 trials in Brazil are being given one dose with the control arm Meningococcal ACYW vaccine
- The Phase 3 trials in the US are being given two doses with saline as the control arm

What do Phase 3 trials tell us?

Phase 3 trials give us preliminary information on efficacy. However, there is no information on the duration of the protection. Will it be 6 months, 12 months, 48 months? This information comes from post-implementation Phase 4 studies and careful monitoring.

Will the vaccines be safe when they are released?

Vaccines are only licensed on strong evidence of safety and protective efficacy. Therefore, we can be confident in them. However, once they are licensed, we continue to learn about them.

Who should get the vaccines?

- The elderly
- Those with chronic medical conditions of lungs and heart, diabetes and hypertension
- Healthcare workers

Start with those. If you are not in one of those groups, you may have to wait your turn.

Will vaccines give lasting immunity?

There is no evidence of loss of sudden loss of immunity after 6 or 12 months or of a particular risk group not responding well

The Hong Kong case of reinfection showed that there was residual immunity that prevented symptoms in the second infection.

So, if a person who has been vaccinated does become infected, “who cares” as it is likely to be mild or asymptomatic – you get a booting effect and protection.

UNDERSTANDING HERD IMMUNITY

This article in [Nature](#) is a great primer on herd immunity, what it is and where we are heading with #COVID19. If you are not comfortable with the maths, just get through the first sentences and it is worth continuing the read.

Concept of herd immunity

Only a proportion of the population needs to be immune (either from having been infected or from vaccination) for an infectious agent to stop generating large outbreaks. Herd immunity is achieved when, on average, one infected person in a population generates less than one secondary case ($R_0 < 1$).

FACE MASKS MAY ALLOW IMMUNITY BY LIMITING VIRUS DOSE AND CAUSING MORE ASYMPTOMATIC CASES

The [New England Journal of Medicine](#) postulates that the universal wearing of face masks may aid the development of herd immunity while increasing the number of asymptomatic cases.

The core of the idea is that the size of the infective dose of virus may determine the severity of the illness, a long-held concept in virology; the lower the infective dose, the less severe the illness.

Supporting this theory, a study in the [Lancet](#) last month found SARS-CoV-2 viral load at diagnosis to be an independent predictor of mortality in a large hospitalised cohort (n=1.145).

We await further studies BUT this is another reason for the wider use of face masks.

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