

### **Heterologous Prime boost in COVID vaccines**

Heterologous prime boost in vaccinology means using different vaccines for the primary and booster shots in an individual. Nowadays, there is a cafeteria style choice of various COVID vaccines. Both advantages and availability of each vaccine is variable. So it may be useful to see what happens when one vaccine is followed by a different kind of vaccine.

The mRNA vaccines induce T-cell mediated immune response which may have a long lasting immunity. The inactivated adeno-viral vector vaccines on the other hand have a more robust antibody response. When two doses of the inactivated viral-vector vaccine are used, it appears that the second dose may have lower responses as the body mounts a response against the vector.

In Europe there are several trials evaluating the effects of using various combinations of inactivated viral vector vaccine and the mRNA vaccine. The Com-Cov study from UK, has four study groups: those who receive both doses of the Astra-Zeneca vaccine, both doses of the Pfizer vaccine, first Astra-Zeneca vaccine followed by booster with the Pfizer vaccine, and the reverse. Preliminary safety data published shows there were more systemic effects like fever following heterologous vaccination 34-41% *vis-a-vis* 10-21% when both vaccines used were same. There were no major adverse effects with heterologous combination. Hematological and biochemical tests done were normal.

The order of vaccines may also make a difference. For example, in trials involving HIV vaccines, giving the DNA vaccine first followed by protein subunit vaccine had best responses. Another strategy is to inject both DNA in plasmid form with recombinant spike protein together in a single shot. This has only been tested in animals so far.

Overall, it appears that combining two different types of vaccine may confer better protection at the cost of mildly increased initial systemic effects like fever. Long term data are still awaited.

(Lancet 29 May 2021)

### **The Pfizer vaccine in adolescents**

Safety, immunogenicity and efficacy data of the Pfizer vaccine in children aged 12-15 years was recently published. This was a multi-centric randomized controlled trial in 2260 adolescents. The main adverse effects were local pain (79-86%), fatigue (60-66%) and headache (55-65%). Higher levels of neutralizing antibody titers were seen in the 12-15 year age group as compared to those aged 16-25 year. No cases of COVID-19 were reported in those who received the vaccine while 16 cases were reported in the placebo group.

This is welcome news for pediatricians all over the globe.  
(NEJM 27 May 2021)

### **Efficacy and safety of the Sputnik vaccine**

This vaccine was developed in Moscow by the Gamaleya Research Institute of Epidemiology and Microbiology. It is an inactivated adeno-viral vector based vaccine. Its first dose has the recombinant Adeno virus 26 (rAd26). The second dose has a different adeno virus vector rAd5 and is given after 21 days. The E1 gene has been removed from the adeno virus to prevent replication. The use of two different adeno viral vectors is to pre-empt any existing immunity against adeno viruses in the community.

Initial Phase I/II data published in September, 2020 had shown adequate safety. They had also shown both neutralizing antibodies and robust T-cell responses suggesting long term immunity. Phase III data in 21970 adults published recently in the Lancet demonstrated an efficacy of 91.6%. Incidence of infections in vaccinated individuals plotted over time showed that by 18 days after the first dose, there was adequate immune response to prevent SARS-CoV-2 infection. Only minor adverse effects were observed. Four deaths noted in the study group were in individuals with severe co-morbidities and were deemed to be unrelated to the vaccine.

A single dose of the vaccine is being marketed as Sputnik light and is considered to have an efficacy of 79.4%. An Indian pharma company has already launched the vaccine in India, and another will soon commence manufacturing the vaccine.

(Lancet 20 February 2021; The Economic Times 27 May 2021)

### **The Millennium technology prize**

Shankar Balasubramanyan, an Indian born British chemist from Cambridge has won the Millennium technology prize for developing one of the fastest DNA sequencing technologies called the Solexa-Illumina platform. As a child he wanted to be a professional footballer but decided later it would be safer to be a scientist.

The idea for the technology was born while brainstorming with his colleagues over several pints of beer in a pub in Cambridge. They came up with an idea to dramatically increase the speed of DNA sequencing 100,000 fold while steeply cutting down the cost. Finally along with his colleague David Klenerman, they founded the company Solexa and the rest is history.

The method involves fragmenting the DNA and immobilizing it on a chip. The sequence is then decoded base-by-base using fluorescent labelled nucleotides. Sophisticated software is then applied to create the final sequence. Today the Solexa-Illumina technology is the most widely used platform for next generation DNA sequencing. This technology has helped in rapidly sequencing the SARS-CoV-2 and subsequently developing effective vaccines.

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