

Memory B cells against COVID 19 persist and evolve with time

A study on the humoral responses in 87 patients with COVID 19 infections by Gaebler, et al. from the Rockefeller Institute is in the news. Both IgG and IgM antibodies levels against the spike protein Receptor Binding Domain (RBD) showed a decline at 1.3 and 6.2 months, though IgA levels were less affected. Further neutralising activity tested using viral assays showed a 5 fold decline.

In sharp contrast, the memory B cells against the RBD showed no decline or sometimes an increase in numbers. A clonal turnover of memory B cells was demonstrated at 6.2 months. Interestingly, the antibodies they expressed showed hypermutation with increased potency against mutations in the spike protein RBD.

The researchers then performed intestinal biopsies of 14 volunteers. They found persistence of viral genome in the intestinal mucosa in 50% of these asymptomatic patients. This fascinating data suggests that the virus may persist in various body tissues like the intestine where the virus continues to mutate and the memory B cells evolve to handle these mutations. Hence our protection after natural SARS CoV2 infection may be much longer lasting and evolving despite viral variation, much beyond 6 months as has been supposed earlier. (bioRxiv <https://doi.org/10.1101/2020.11.03.367391> (2020); *Nat Rev Immunol.* 2021)

Guidelines to prevent infant food allergies

There have been several high impact RCT's published recently about strategies to prevent food allergies. They include LEAP (learning early about peanut allergy), EAT (enquiring about tolerance), STEP (starting time for egg protein) etc. They have resulted in a paradigm shift in the way we could potentially prevent food allergies.

The story starts in the 1990's when it was noticed that peanut allergy had doubled in children in Western countries over a period of 10 years. Peanut allergy starts early in life and is the leading cause of anaphylaxis and death in children in the West. Guidelines in UK (1998) and the US (2000) recommended that peanut be excluded from the diet of children upto 5 years of age, if they were at high risk for food allergies. But astute clinicians noticed that peanut allergy was 10 times higher in Jewish children brought up in UK versus those brought up in Israel. On questioning, they found that Israeli children were introduced to peanut much before 6 months of age. Hence it was hypothesized that perhaps early introduction to certain foods may help do develop tolerance to various foods.

This has been best studied for peanut allergy. In the LEAP study babies at high risk for allergies such as those with severe

eczema and egg allergy were introduced to peanut paste between 4-6 months of age. Compared to controls in whom peanut was avoided till 5 years of age there was an 86% reduction in peanut allergy by 5 years. Since then there have been several well conducted studies which have borne out this hypothesis.

Hence the AAAAI (American Academy of Allergy, Asthma and Immunology) has brought out a consensus guideline about this. They have suggested that babies with severe eczema or family history of atopy may be introduced to peanut containing products between 4-6 months of age. All infants, even those without risk for allergies may be introduced to cooked egg products between 4-6 months. Other potentially allergic foods like soy, wheat, tree nuts and fish may also be introduced early. They suggest that introduction to a diverse foods early in infancy may be beneficial in preventing food allergies. They have no data to suggest that hydrolysed formulas could prevent food allergies.

Parents may introduce 1 food at a time every 3 days. Evidence for developmental readiness to handle complimentary foods include holding the head up when sitting, showing interest in what others are eating and opening their mouth when food approaches.

(*Allergy Clin Immunol Prac.* 2021)

Second generation COVID vaccines

So far the vaccine roll out has been fairly safe but several questions about the eventual effect of the COVID vaccines still remain. One scenario is that the vaccine recipient is protected but he becomes an asymptomatic carrier, continuing to spread the disease. More dramatically if the vaccine recipient subsequently contracts COVID19, could he develop a worse disease by a mechanism of antibody dependant enhancement? The mRNA vaccines have shown excellent protection but fall short in the requirement for extremely low temperatures in the cold chain. Scientists therefore are continuing to develop newer vaccines.

The Imperial College of London is developing a self amplifying mRNA vaccine which will not need a booster. Researchers in Maryland- based Novavax are developing a genetically engineered protein subunit vaccine with a saponin based adjuvant. Another unique approach is using nanoparticle of the receptor binding domain which has been shown to elicit a ten times higher antibody response than when the entire spike protein is injected. Closer home, Bharat Biotech has received approval to conduct phase I trials on 75 individuals of its nasal vaccine which will also not require any booster.

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