

Corona Virus and COVID-19 Ten Months Later

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We are now more than 10 months into what has shaped up to be an ongoing, and growing pandemic of the novel coronavirus SARS CoV2. What have we learned during this time, and what does it mean for people with VCFS?

As expected, we now know that people with certain immune deficiencies are definitely at higher risk from the virus. Furthermore, we have learned a lot about this virus and what it does to a normal host. Fascinatingly, the virus itself is capable of suppressing the immune system, and this seems to be a major feature of infection. There are several things that have been shown in patients with COVID-19, such as:

- Low T cell counts; the lower the count, the worse the infection
- High levels of some inflammatory markers – the immune system seems to be ramped up, but obviously not in the direction of killing the virus (which would need T cells)
- Low levels of some early immune proteins called interferons
In the sickest patients, low immune responses against the virus
- Immune responses (antibodies) that don't last long after infection as cleared

All in all, it paints the picture of a virus that redirects the immune system away from it, and the more successful it is at doing this, the sicker the patient becomes. A lot of the proteins that have been linked to this ability likely evolved so the virus could co-exist with bats, which have very high levels of interferon naturally. Humans do not, so when the virus turns on its anti-interferon genes our immune system cannot cope.

Unfortunately, this means that people with VCFS may be at higher risk from COVID-19 even than some other immune deficiencies. Although more people with VCFS have reasonable T cell function, many have low T cells numbers to start with, and some do have a degree of dysfunction. Because there isn't a lot of natural immunity to COVID-19, it is unlikely that those receiving immune globulin replacement in the form of IVIG or SCIG will get much protection.

This means that a general recommendation to avoid crowds and to wear masks is really the best way to protect anyone with VCFS against the virus, for now.

So, what's the silver lining? Well, there are actually several very promising vaccine candidates that are likely to offer protection even to people with VCFS, and safely. Several of the lead candidates (e.g., the Moderna and Pfizer vaccines) are mRNA vaccines, which are made from small genetic strips of material that the body can use to make viral proteins, called mRNAs. Because of the way mRNA is handled by the body, they could end up producing strong immunity against the virus, including T cell responses, but without the risk of a real infection or the interferon-reducing genes of the full virus. Vaccine-induced immunity may be better than

natural immunity to this virus! There are also other killed or subunit vaccines such as the Oxford vaccine that also seem to induce strong T cell responses and will probably be safe for people with VCFS, as the viral vector used to carry the SARS CoV2 proteins has been engineered to render it unable to live in humans.

These are just three of the possible candidates, but all are in late-stage phase III studies and one or more of them may end up approved within the next 6-12 months. It is important that we trust the efficacy and safety data coming with these vaccines for when they are approved, and all the major vaccine manufacturers signed a joint statement that they would not rush a vaccine to market that was not properly investigated. At this time, it's impossible to know which vaccine will be first, and whether it will work well in patients with VCFS – but as more data is published that will hopefully become clear. For my part, I have signed up to be a subject in a vaccine clinical trial, so a very small part of the data used to make these decisions will come from me!

Until we have a vaccine, and this is under better control, please stay safe – practice social distancing and wear a mask and take this virus seriously.