The SARS-CoV-2 variants of concern

As the SARS-CoV-2 pandemic unfolds, the new villains in the drama are 3 viral variants of concern (VOC) which have recently emerged. The B.1.1.7 was described in the UK. The B.1.351 surfaced in South Africa and P.1 was born in Brazil. What do we to know about these viral variants?

All the three variants have the N501Y mutation in the receptor binding site of the spike protein. The B.1.351 and P.1 also have two additional mutations which again affect the receptor binding domain. These mutations have resulted in increased binding to the ACE 2 receptor and subsequently higher infectivity. The British variant is 36-75% more contagious. The South African variant is 50% more transmissible. Early data from Brazil suggests that the P.1 is 2.5 times more contagious.

What about disease severity? Initial studies suggested that the UK variant, B.1.1.7 did not cause more severe disease. However, more recent data, suggests that the mortality is more in the new variant. The mortality hazard ratio in the new variant as compared to the old was 1.64 (95% CI 1.32-2.04). This translates into a death rate of 4.1/1000 cases for the new variant against 2.5/1000 in the old variant. In South Africa, the mortality due to the new variants was 20% more than the previously reported death rates. It could also be due to the rapidly overburdened health care system.

The million dollar question which remains is whether vaccination or previous infection will protect against the new variants. Sera from individuals immunized with the Moderna vaccine showed that they efficiently neutralized the UK variant B.1.1.7. Its efficacy was slightly reduced for the South African strain but will probably be effective clinically. However, Moderna has announced that they will develop a new modified vaccine which will be effective against the new strains.

Serum from patients vaccinated with the Pfizer- BionTech vaccine also had a slightly lesser efficacy in neutralizing the new variants but the vaccine will probably remain clinically effective. Serum from patients vaccinated with the AstraZeneca vaccine failed to neutralize the new variants.

Initial data suggests that natural immunity due to previous infection with the old variant is partially effective in preventing infection with the new UK strain but hardly effective in preventing infection with the South African strain. More concrete data is awaited.

(*New SARS-CoV-2 variants- Clinical, public health, vaccine implications. NEJM 24 March 2021*)

mRNA vaccines- transforming medicine

In addition of their sucess against SARS-CoV-2, mRNA vaccines are also in the race to treat several non-infectious disorders.

It was known for decades that mice injected with mRNA could produce the proteins that the mRNA coded for. However, the mRNA itself produced a severe inflammatory response. Secondly, the mRNA would get degraded very fast in the body, which led to low levels of protein production.

The major breakthrough came from the work of a pair of scientists from the University of Pennsylvania - Katalin Kariko and Drew Weissman. They found that using synthetic nucleosides to produce the mRNA prevented the inflammatory response and also resulted in more protein production. The next milestone was the imaginative use of lipid nanoparticles to coat the mRNA. This prevented the rapid degradation of mRNA.

When the COVID-19 pandemic swept the world, we needed a safe vaccine which could be rapidly developed at low cost. mRNA vaccines ticked all the boxes.

Now, Ugur Sahin, CEO of BionTech and his group have published another remarkable piece of research. They developed a mRNA which delivers auto antigens of multiple sclerosis into the lymphoid dendritic cells. This activates a regulatory T cell which inhibits the inflammatory response against the targeted autoantigens. In mouse models of multiple sclerosis, this mRNA vaccine delayed the progression and reduced the severity of the disease. Most importantly, unlike the regular therapy of multiple sclerosis it does not induce generalized immunosuppression.

So besides its potential role in emerging infectious diseases, mRNA vaccines are purported to be the next blockbuster in the therapeutic arsenal against chronic diseases like cancers, cystic fibrosis and heart disease.

(*Krienke et al. Science, 8 January 2021*)

Nightingale wards

Florence Nightingale pioneered the idea that the design of hospital wards had a critical impact on the well-being of patients. The so called Nightingale wards had large windows, which allowed fresh air and sunlight to flood the rooms. Steven Lockley who studies circadian rhythm and sleep in Harvard Medical School has discussed how right Nightingale was when she highlighted the role of natural light in human health and well-being.

Patients in rooms with good natural light and outdoor views have been shown to recover faster with fewer painkillers. Heart rates, blood pressure and mood is better in these patients. Rods and cones were initially considered to be the only cells involved in visual inputs. It is now well established that non visual photoreceptors in the retina modulate our circadian rhythm, mood, alertness and cognitive functions. A large study from Korea analyzed length of stay of patients admitted with a bed next to a window versus away from a window. Patients with beds next to a window had much shorter hospital stays.

The COVID-19 pandemic has further emphasized the need for sunlight and cross-ventilation. There are many factors we need to consider while treating patients, and hospital design is often neglected.

(What Florence Nightingale can teach us about architecture and health. Scientific American 18 March, 2021)

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