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Covid-19: New Developments in Vaccines and Testing

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We have now been living with Covid-19 for over 8 months. The initial measures that we had to understand were relatively straightforward including handwashing, social distancing, and lockdown directives. We are now being challenged by new, more sophisticated concepts. These include vaccine developments and the new array of testing choices.

The race to produce a Covid-19 vaccine continues to gather pace. The U.S. government launched 'Operation Warp Speed (OWS)' on May 11th, 2020. It is a partnership between the Department of Health and Human Services, the Department of Defense, and the private sector. It has pledged $10 billion to deliver 300 million doses of a safe and effective vaccine by January 2021. The term 'warp speed' was popularized by the TV series Star Trek, where spacecrafts could travel at speeds greater than the speed of light by many orders of magnitude[1].

The aim of the project is to do with speed without sacrificing on safety. The U.S. government will take on the financial risk while avoiding harm. Normally pharmaceutical companies do not manufacture hundreds of millions of doses of a vaccine until they get FDA approval. This time, parallel processes are in operation. Manufacturing to scale is taking place while the safety and efficacy trials continue. If it works, it will save 6 – 12 months of time in the production of a Covid-19 vaccine. If it doesn't work billions of dollars will be lost[2].

In normal circumstances it can take 10 years to bring a new vaccine to the market. The fastest vaccine to be developed was the Mumps vaccine which was developed in 4 years. There are many phases and speed bumps in production of a product. Phases 1 and 2 involve small numbers of participants. The purpose is to test the safety and immune response to the vaccine. The pointers include antibody response, T cell response, and neutralization of wild type virus[3]. Phase 3 tests the efficacy in thousands of individuals. This phase is important to determine how effective the vaccine will be in preventing the disease. If it works, the next question will be for how long the vaccine will provide protection.

There are 8 vaccines in the OWS portfolio. These vaccines had to use one of four vaccine technologies in order to be considered. The platforms were mRNA, replication-defective live vector, recombinant-subunit-adjuvant protein or the attenuated replicating live-vector type[1]. The following three vaccines have received some prominence and are better known[4]. There is the AstraZeneca collaboration with the University of Oxford. The vaccine is a SARS-CoV-2 spike protein. It is a viral vector vaccine, which uses a modified adenovirus as the vector. So far it has triggered a strong immune response with increased antibody levels and T cell reaction.

The side-effects have been minor, fatigue and headaches. In phase three, 50,000 participants will be recruited across the U.K., Brazil, U.S. and South Africa. Moderna is a Massachusetts-based biotech company that is working in collaboration with the NIH. It is an mRNA vaccine. If successful it would be the first mRNA vaccine approved for human use. The Moderna phase 3 trial involves 30,000 U.S. participants. Pfizer in collaboration with the German biotech company BioNTech has developed an mRNA vaccine. They are doing a combined phase 2/3 trial involving 30,000 participants across Germany, Brazil and Argentina.

The vaccine approval process will be a major challenge. The FDA stated that the evaluation processes will be based on the science and the data. Safety and efficacy are key requirements. If the approval process is not thorough, the acceptability of the vaccine will be damaged. It is a big task to be able to combine speed, accuracy, and balance.

WHO has recently stressed the point that a weakly effective vaccine (reducing the Covid-19 incidence by only 10-20%) could actually worsen the pandemic[5]. It would create false reassurance leading to the relaxation of other measures. A successful vaccine should show an estimated risk reduction of at least one-half, although more would be better. The example quoted of a satisfactory outcome is an evenly randomised trial with 50 cases arising in those vaccinated, and 100 cases arising in those given placebos. A vaccine that has 50% efficacy would appreciably reduce the incidence of Covid-19 and provide useful herd immunity.

Many medical commentators are concerned about the press release culture in relation to Covid-19 at the present time. If the initial headlines are over-optimistic, it can damage trust when there is a subsequent need for revision. The medical and scientific community must try to do a better job of communicating uncertainty. This is why the word 'balance' is so important.

There remains much discussion about the testing methodology for the SARS-CoV-2 virus. Nasopharyngeal swabs have historically been considered the reference method for respiratory virus detection. However, it is labour intensive and requires health care workers (HCWs) and personal protective equipment (PPEs). The other methods, anterior nasal swabs (ANS) and saliva specimens are being considered. The advantages of ANS and saliva are that they less invasive, more suitable for children, and have the potential for patients' self-collection.

A study[6] from the Meyer Children's Hospital, Florence compared paired samples of nasal and oropharyngeal swabs taken every 1-3 days on a group of 11 children with proven Covid-19. Among a total of 52 paired specimens, 24/26 of the nasal swabs were positive, and 20/26 of the oropharyngeal swabs were positive. The authors concluded that the nasal swabs were superior.

The other testing method is the use of saliva specimens to identify Covid-19 infection. Preliminary findings show promise. In 70 patients with confirmed Covid-19 infection, saliva sample were taken. In all cases the saliva tested positive for SARS-CoV-2. In another exercise 495 asymptomatic health care workers provides saliva samples for SARS-CoV-2. There were 13 positives. All were confirmed on nasopharyngeal swabs[7].

A Utah study compared nasopharyngeal swabs (NPS) with self-collected anterior nasal swabs (ANS) and saliva samples among 354 adult participants. The positive agreement rate between NPS and saliva was 93.8% and the positive agreement rate between NPS and ANS was 86.3%. The negative agreement rates were 97.8% and 99.6% respectively[8].

However, one of the potential problems about saliva testing is the presence of food particles in the sample. This can affect the technology and lead to reruns. The saliva protocols require the avoidance of food, water, and tooth brushing prior to testing and/or rely on RNA stabilization reagents as part of the collection device. ANS may also be preferable to a saliva test in a young child, as febrile toddlers won't open their mouths for sufficient time to take a salivary swab (R. Drew personal communication).

The coming weeks and months will undoubtedly witness further developments in the strategies against Covid-19.

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