

COVID19 Advisory 16 “Wide-eyed in November”

The week of 9th- 16th November 2020 was awesome! Professor Constantin Coussios presented a stunning lecture to IESF BS. On the same day Pzifer BioNTech announced a novel mRNA Vaccine for COVID19. Seven days later Moderna announced its own Vaccine (mRNA1273). In between, Jane and I attended the 50th Royal Society of Medicine COVID19 Webinar “Vaccines: Living with the Virus” and I also learned about ‘COMRADES’.

RSM President Sir Roger Kirby, distilling more than 100 questions from Members, interviewed Professor Sir Jeremy Farrar FRS, Director of the Wellcome Trust and formerly Director of the Oxford University Virus Research Department in Saigon.

In his first question, he asked Prof. Farrar whether he believed we have arrived ‘at a fork in the road’. Could things return to normal by next Spring as Sir John Bell, Regius Professor of Physic at Oxford, had affirmed on the Today Programme Radio 4? In reply, he quipped that Prof. Bell is a Canadian, and Canadian Springs can last a long time!

On flights to and from Rochester Minnesota, below the Canadian border for my one year Residency (April 1981 to March 1982) at the Mayo Clinic, I recall the deep winter snow!

Prof. Farrar reflected that even in late January 2020 none of us could have predicted the massive disruptions ahead. All this had caused him to feel a little gloomy. But the way forward is through Science and Innovation, he urged. Not pure Science only, but all the disciplines – Behavioural, Bio-Medical, Psychological and Sociological. As if to illustrate this passionate view, along comes good news about the mRNA vaccines. Oxford

is using a familiar vaccine production by growing the harmless carrier virus, already existing in nature, in egg albumen, whilst mRNA vaccines are a completely novel technology.

Together they sit in the “First Eleven” portfolio, leading vaccines already well advanced in Phase 3 trials. We can expect more news in the next one to two months. He cautioned that there are still challenges to come - “Hope in a vial” is still short of “getting it into somebody’s arm”. All these vaccines will need two doses and different vaccines may suit different populations and climates. Schedules should not be mixed but we should stay **pluralist** in our thinking.

Prof. Kirby then asked questions on Equity, Distribution and Concerns about Big Pharma *hanging on to the ‘secret sauce’ (source?!)*. Prof. Farrar declared his complete confidence in the National Regulators and his determination that we will not deny other people good things while we ourselves seek better.

To sustain future research progress, Prof Farrar declared that there must be some element of Public Sector funding. Governments need to issue Guidance indicating what they need – *and will support*. For example, we desperately need new classes of antibacterial drugs to cope with MRSA (Methycillin resistant Staphylococcus aureus). The present funding models need to change. At the same time, there must be respect and protection for intellectual property.

Prof. Farrar declared that 2020 is a year of “Disruptive technologies” (*I had to look up this*

use of the word – disruptive. **In Business Theory**, an innovative technology which creates a new market and an added value network, such as satellites, e-commerce or genome sequencing, is termed **disruptive**). The curtain has been pulled back. Science has arrived at that fork in the road for many classes of therapeutics. “This good news about Coronavirus will *also be a proof of concept* for a promising way of warding off a whole menagerie of diseases from HIV to Melanoma through the body’s own fortification”* (Times 10th November refers). mRNA vaccine research development is built on the back of research into the treatment of cancer and could perhaps influence the treatment of mental health as well. There is a prospect of blurring those margins.

“A home run for mRNA Technology” said the Chief Medical Officer of Moderna, a Company which was launched only 10 years ago and has never before brought a product to market. The US Dept. of Health Services – *delivering a “Flag Ship Vaccine Programme – Operation Warp Speed”* – has backed Moderna with \$2 bn. *(Financial Times. 17th November 2020 refers).

The Moderna trial of 30,000 subjects reports 95 subjects developing COVID19. Only 5 had been given the vaccine, a vaccine failure rate of $5/15,000 = 0.03\%$. Proof of the vaccine *stopping* the infective wave will take 6 months more. Some Moderna mRNA1273 Logistics are; shipping and storage at -20deg. C., a “shelf-life” of 6 months and, once thawed, stable for 30 days. The UK Govt. has ordered 5million doses for 2020 and 30 million in 2021.

BioNTech, founded in 2008, has a technically ambitious manufacturing process, compared to the carrier virus adaptation. It involves isolating the mRNA spike fragment and bundling it into a microscopic blob of fat. This process is well suited to mass production but there are substantial ‘Cold –chain’ issues; nitrogen storage at -70deg.C.. Once thawed, it is only stable for 5 days when kept in GP Practice – grade fridges.

The Pfizer BioNTech partnership aims to have one hundred million doses ready to go by the end of this year**. Their Phase 3 study began in July, recruiting 43,000 subjects. After 3 months, 94 subjects had developed COVID19. Only 8 of these had received the trial vaccine (0.04%).

The UK Govt. has ordered approximately 96 million doses. Another source claims 5 million in 2020, 30 in 2021! Until there is FDA and MHRA (Medicines and Healthcare products Regulatory Agency) approval, there will be no vaccines for the UK.

Prof Farrar expressed some strong views for the year 2020. The ledger of American contributions is especially strong *through its Institutions* but undermining these is very dangerous for the world.

As for Coronavirus, it is now established as **Endemic- a part of humanity**. (I first heard Prof. Farrar use this term back in June). He describes himself now as feeling much more optimistic – there is a ray of sunshine. He believes in Science, the Scientist and Global Endeavour. **The things we need to change are global. Epidemics are the horrible poster child for**

‘Steady as she goes’. We must stop flirting with the party political, the nationalistic behaviour, and nationalism.

No previous year in the last one hundred has seen Science more engaged with the Community and it must not retreat again into its Ivory Towers. The Sciences can bring humility and assist in the avoidance of promising more than can be delivered. Prof. Farrar was loud in his praise for Professors Whittey and Valance, who ‘deserve great public thanks’. **SO WHAT ABOUT COMRADES?** The Cambridge Independent (11-17th November) featured the finalists for their Award of Science & Technology Researcher of the Year. Amongst them are Dr Omer Ziv, Cambridge University and his collaborators, some at Justus-Liebig University in Germany. They report revealing “the interactions in SARS-CoV-2 that enable it to infect us.” (Journal Molecular Cell)

Coronavirus has the largest RNA genome known in nature. Much of the information necessary for the virus to infect and reproduce lies in the *viral 3D structure within the cell*. Quite apart from the spike protein (much targeted by prospective vaccines) it is *the shape of the RNA molecule that is critical to its function*. Disrupting the 3D architecture of a viral RNA chain within the host cell will disable some of its functions - perhaps including its ability to reproduce.

New tools enable the understanding of the network of connectivity, opening the way to designing ways to target the virus effectively with therapeutics. **COMRADES stands for Cross-linking Of Matched RNAs And Deep SEquencing**. Developed in 2018 initially to understand the Zika virus, it is able to measure the structural diversity and capture both short and long-range base pairing! **Now that’s what I call ‘Disruptive Technology’!**

As I edited this piece, I had to include more big news stories.

On

19th November 2020, Lancet published a preliminary report on the Oxford Group Phase 2 Trial on 506 healthy adults. Comparing age brackets, 18-55, 56-69 and 70+ showed a *similar strong immune response in all 3 groups*. Vaccination was very well tolerated. Professor Andrew Pollard (Radio 4) explained that the Oxford design principal is to develop a vaccine capable of worldwide distribution - *‘impact is what matters – to reach multiple populations and achieve high coverage’*. *We are still in the foothills of disease control, approaching base-camp! The prospects will be improved if we understand the peculiar characteristics of each different vaccine.*

On 23rd November 2020

*we cheered the news of the Oxford/AstraZeneka vaccine trials across the UK, South Africa and Brazil. Manufacture is well under way and UK vaccination should begin in December. So, pop it in the domestic fridge (2-8 deg. C), **dose small then larger and it will protect 70% or better. Let the global impact and high coverage begin!***

David Hughes

President

23rd November 2020