NOTE OF MEETING – SAG BRIEFING – 23 July 2020 – 17:00 – 18:00

1. First Minister welcomed everyone to the meeting, thanked Professor Sir John Bell for giving up his time to speak to the Group, and then handed over to Professor Andrew Morris.

2. Professor Morris outlined Professor Bell's experience and background as Regis Professor of Medicine at Oxford and his key work as an immunologist, before handing over to Professor Bell for his presentation.

3. Professor Bell thanked the Group for having him along to present. He stated that the immune response to the virus is crucial in preventing and controlling it and therefore there is a need to understand the immunology. A common misperception is that that there has been no pandemic since 1918, however Professor Bell cited 8 close misses, including swine flu, Ebola, 2 outbreaks of SARS and MERS in the Middle East, and suggested this virus will remain an issue going forward. Professor Bell provided background into how the coronavirus is a member of a big family of viruses, explaining that a simple head cold in the winter is very likely to be coronavirus, an endemic type. Covid-19 is a SARS-like coronavirus with a particular set of characteristics, carried by large groups of animals, particularly bats and pangolins. It is, therefore not a straightforward and simple task to gain a better understanding of immunity before Covid-19. The immune system response is not the same.

4. In an innate immune response our cells can be triggered to produce antivirals. The body produces interferons, however Covid-19 is very good at not activating the interferons. Only very small amounts of interferons may be produced, however the virus is adept at avoiding those. There has been some success when people are inhaling interferons and overcome some of the defects and it looks promising that this may be able to deal with the virus.

5. Most of the focus has been on B Cell antibodies. By day 1 or 2 patients show an IgM (immunoglobulin) response and by days 8-14, IgG. The idea was to use antibodies to check who has been infected but the reality is you can't necessarily use Ig levels to identify those who have been infected. The first problem is that initially all tests for detecting antibodies had been found to be sub-optimal, however there are some solid antibody tests out there now. There is ongoing work on home based tests in Oxford, where tests are just being completed.

6. Data from lab based tests were published 10 days ago. As more and more tools are being developed we are able to understand more. Antibodies though are not a 1-2-1 correlation, as you can be swab positive but antibody negative. It has also been found that the antibodies detected are not very enduring – they fall off much more rapidly than, for example the SARS 2003 antibodies. Estimates are they fall off at 30% a month from the 28 day exposure which could result in them disappearing within 6 months. Memory B cells can however last many years. Professor Bell issued a health warning around antibody testing.

7. The third arm of the body's response is cellular response – CD4 and CD8 T-cells, come along and kill the infected cells. Having antibodies provides a certain level of protection but T-cells are durable. The T-cell responses may begin to explain some of the coronavirus puzzles.

8. Professor Bell is of the view that we all have a certain amount of immunity to this virus, which of course has implications for the R-naught. As we are not a naive population it can explain differences in the spread of the disease. As we know people who do badly are the elderly and those with co-morbidities (obesity, diabetes and hypertension). The recently published ONS study shows 70% of positive cases are asymptomatic. Most of us have T-cell immunity. It is also well known that T-cell immunity fades in the elderly – T-cell senescence. This may well account for why not everyone is so ill when they contract Covid-19.

9. In Vietnam there have been 300 cases of Covid-19 from a population of 100 million people with zero deaths. As it has been determined from a study of bats and pangolins (most populous in Vietnam) the spike protein it may be that Vietnamese have been exposed to various coronaviruses that are similar to SARS-CoV-2 over a longer period of time and, therefore have not been so affected by this pandemic.

10. In terms of a vaccine Professor Bell stated things were looking pretty successful in the UK. We are well set up to manufacture and test, and make sure supplies are available.

Adenovirus-based vaccine – this is the basis of the Oxford vaccine led by Prof Sarah Gilbert and colleagues, in conjunction with AstraZeneca. They're seeing good safety and immunogenicity data, including T-cell response. A Janssen one in trials looks hopeful too. Janssen adenovirus-based vaccine is due to go into man next week

Nucleic acid vaccines – easy to construct, but very difficult to manufacture at scale. Nevertheless, they have interesting immunogenicity results.

Protein adjuvant – historical mechanism of vaccine manufacture, GSK focused on this.

In terms of timescales Professor Bell estimated late September/October, once efficacy is determined, that by making some adjudication there could be vaccines before Christmas. Professor Bell stressed this was not a profiteering exercise and it was important that there was a global push to get us all vaccinated.

11. Potential of a second wave – Professor Bell thinks that although we are more diligent in Scotland not everyone elsewhere is social distancing or using face coverings, therefore he feels the risk of a second wave is quite high.

12. Test/Trace/Isolate – we need saturation testing. As most people are asymptomatic, Professor Bell feels testing needs to go up to another level. In the short to medium term we will get over the bumps and get a vaccine, however long term it will never go away. We will get a little bit of immunity but no-one should rest on their laurels. There are likely to be problems with lungs, heart, kidneys and brain over time. So saying that work started on this in January and we have come a long

way in these last 6 months. Scotland has played a crucial part in the development of test and identification of a flow test and is very involved in clinical trials. Professor Bell is pleased there is a highly integrated bio UK all working together on this pandemic.

13. **Questions and Answers** – Professor Morris invited questions from the meeting participants which are detailed below:

First Minister

Q. In terms of B cell immunity, does that start to teach us anything? How do we deal with this virus in the short term?
Q. How optimistic is optimistic? In advance of a winter second wave what is the estimate of good a solution will there be pre-winter?
Observation – we have an effective test/track facility, however that is based on symptomatic. If we continue with that we will be left with a vulnerability.

Professor Bell

A. Antibodies eliminating the virus. What do the tests really mean? Can you fight off a second exposure? I think probably, but I have no evidence to back that up. We need to find out if there are different levels of infection. We also need to look at T-cells too.

A. On the vaccine, the truth is you are never sure until you are there. The immunogenicity data is a good as we can expect, so you be at least be able to reduce, if not eliminate. 75%-80% likely you will get something that works. Again no one single vaccine will be the answer. Numbers needing to be vaccinated are around 3.5-4 billion people. The highest number done so far has been 260 million. So now is the time to start thinking about how you will deploy the vaccine, who will you prioritise to receive the vaccine? Health care workers, then whom? Will you vaccinate children?

A. On your observation - a test/trace based on folks with no symptoms is not going to work. The Dutch are testing sewage. We need to be large scale testing and we need to get our skates on. It will be bad if winter flu and Covid-19 are still around. We need testing levels up to a million.

NR

A. Scaling of capacity is a must.

Deputy First Minister

Q. What are your thoughts on priorities for antibodies expansion?

Professor Bell

A. For the moment, because there's 6% positivity in Scotland, I wouldn't do antibody testing. Need to focus on PCR testing of the virus. There is a question of

would wider spread testing with lower sensitivity (e.g LAMP) be better than fewer tests with better sensitivity. You could have 99% sensitivity in 1 million tests or 70% sensitivity in 5 million. But clearly everyone will want the 'good' test and that's when we get into the realms of behavioural science. But there's surface acoustic wave testing available – results in 3 minutes, scans very large numbers of people - we need to keep exploring testing methods.

Nicola Steedman

Q. Have we seen anything globally on reinfection? Do folk re-infected get less severe symptoms? Should we allow non-vulnerable people to get the virus?

Professor Bell

A. That is a very tricky situation. How, for example, do you stop young people coming into contact with elderly/vulnerable?

NR

A. There is not a lot of evidence of re-infection globally.

Professor Bell

A. There should be a challenge study on neutralising antibodies and that will answer the question definitively.

CMO

Q. The testing of asymptomatic cases need to be though about. In reports about chronic effects, is there a plausible reason for immunology? Is it acute phase damage?

Professor Bell

A. Because it binds to the ACE2 receptor, you have autoantibodies (ie antibodies that attack our own cells) being made when the body responds to it, which in turn bind to other ACE2 receptors NR at Hopkins is looking at this. Maybe it is an ongoing inflammatory condition, perhaps we could use cyclosporine to suppress it?

Professor Jill Pell

Q. How is the BAME community affected, since their risk seems to be higher even after taking account of cardio metabolic risk factors?

A. There is a genuine risk factor although it appears to be more so for South Asian rather than African Caribbean and we don't know enough yet on what is going on there. For further shielding work we need to pay close attention to that group of people.

Professor Andrew Morris thanked Professor Bell for his time and said there would be a further invitation extended to him in 2-3 months to come back to the Group again.

NR mentioned the asymptomatic testing focus and asked who is leading in Scotland on this as he is keen to ensure a 4-nation approach. Professor Morris took that as an action and the meeting closed.

SGoRR Team Leader

23 July 2020