

CORONAVIRUS



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It is impossible today to be unaware of the Coronavirus pandemic that has swept across the world since the beginning of 2020. Just over one hundred years on from the 'Spanish flu' of 1918-1920, the world faces similar challenges from the COVID-19 disease at a time when we enjoy much more advanced medical treatments and practices but have also enabled the spread of the disease through greater global connectivity.

SARS-CoV-2 is the virus that causes the disease, COVID-19. The coronavirus family includes a number of viruses which cause a range of illnesses from the common cold to the Severe Acute Respiratory Syndrome (SARS) epidemic in 2002. There are also hundreds of other strains of Coronaviruses which infect non-human species, notably bats. Like humans, bats live in close quarters, so easily spread pathogens between each other, and as humans begin to encroach on their habitats, this makes cross-species transmission a particular risk. Whilst the genetic makeup of SARS-CoV-2 points towards the original virus being bat-borne, evidence suggests that it may have been transmitted to humans via an intermediate species¹. In 2016, following the Ebola epidemic, the World Health Organization (WHO) identified the SARSr-COV virus family as having potential for a future epidemic and recommended research into diagnostic tests, vaccines and medicines.

The origin of the novel Coronavirus is Wuhan in China, with a population of over 11 million people. The first confirmed case was recorded on 1 December 2019, but it is speculated that the real first case might have been contracted earlier in November 2019. Once more cases were discovered,

samples from hospitalised patients were analysed at the Wuhan Institute of Virology where the virus was later isolated and identified as a novel coronavirus. China officially notified the WHO of cases of pneumonia with an unknown aetiology on 31 December.

Spread of the virus has been rapid. The first COVID-19 case outside China was announced in South Korea on 8 January. By 31 January, the first UK case was confirmed. Four weeks later, on 28 February, we documented the first case of infection transmitted within the UK; all previous cases had been infected abroad. Within one month, there had been over 22,000 cases and 1,408 deaths in the UK². During this time, other regional epicentres of disease have emerged, noticeably Italy, Spain and the USA. In mid-March, the UK Government began to shepherd the largest expansion of state power outside of wartime through Parliament, legislating to restrict the movement of the UK population and ensure they remained at home except for essential work, exercise, or shopping for food or medicine.

This came as the Government moved away from a policy of building herd immunity. Herd immunity occurs when a large proportion of the population is protected against a particular

disease, preventing its transmission through that population. This can be achieved either through vaccination or when enough people in the population have built up antibodies by fighting the pathogen directly. However, this latter strategy only works to reduce serious disease if, when building that immunity, vulnerable individuals are protected from contracting the virus. If not, the consequences could be severe. As SARS-CoV-2 is a novel virus in humans, it is not yet known how long the immunity built up would last for. Some other viruses in the Coronavirus family that cause common colds build immunity that only lasts for a few months, but this may be related to their co-evolution with the human immune system. Given the uncertainty of the characteristics of this novel virus and how it would interact with the human immune system, the current strategy which will allow herd immunity to be built up slowly together with avoiding exposure of overly vulnerable parts of the population, such as the elderly or the immunocompromised, is to be welcomed.

This new strategy includes a 'delay' phase to slow the spread of COVID-19 after containment measures were no longer feasible. This was aimed at lowering the peak impact and push it away from the winter

season in order to prevent the NHS from becoming overwhelmed. The delay also buys time for research to better understand the course of the disease and to innovate medical responses such as diagnostics, drugs and vaccines.

SARS-CoV-2 is a relatively infectious virus: a person with seasonal flu typically infects 1.4 other people, so if this happens 10 times, then around 29 people will become infected; a person infected with SARS-CoV-2 will typically infect 3 other people, so if this happens 10 times, then approximately 59,000 other people will become infected. This has naturally led to focus on developing a vaccine, a process that most experts believe will take at least 18 months. This timeframe has been facilitated by China sequencing the genetic

UKRI, has begun advertising for human volunteers for trials. It will use an adenovirus vaccine vector, which was chosen as the most suitable candidate because of its capability to create a strong immune response in an individual and for its non-replicating nature, meaning it will not cause an ongoing infection in a vaccinated individual. Coronaviruses have spike shaped proteins on their surfaces and other studies have suggested that this part of the virus is most likely to invoke an immune response. The Oxford vaccine uses this by producing the SARS-CoV-2⁴ spike protein in the vaccinated individual, priming their immune system to attack the virus if it later infects the body.

Conventionally, vaccines have used live, attenuated forms of a virus, or a part of it, which have

into vaccines. No vaccine made from genetic material has yet been successfully approved for human use, however, and it is crucial, both for successfully resolving this pandemic and for future vaccine confidence, that we are not tempted by shortcuts and follow the rigorous safety protocols that govern the approval and manufacture of new pharmaceuticals.

The route that vaccines take from laboratory to clinic is an arduous and long one. Vaccines are risky commercial investments: with so few successfully emerging from clinical trials ready for the market, pharmaceutical companies often prefer to place safer bets with drug development. Indeed, a vaccine against SARS-CoV-2 is by no means an assured certainty. The infrastructure for vaccine

widespread manufacture of a vaccine. In 2018, the Government announced the funding of a new Vaccine Manufacturing and Innovation Centre at Oxford that will be able to carry out vaccine manufacturing at a variety of scales.

Through better understanding of the virus and how it interacts with the immune system, we have a better opportunity to look to developing effective therapeutics. This includes the repurposing of existing interventions that work in the treatment of other illnesses. The UK Government has been active in using rapid response research funding to back this sort of research, including an adaptive trial at Oxford currently looking at two drugs currently used to treat HIV. This is a strategic move that may pay extraordinary dividends if the vaccine research does not deliver the desired results in the appropriate timeframe.

The UK is one of the international partners at the forefront of immunological research. Through the commitment of the international immunological community to share new research information without delay and to jointly conceptualize new avenues for treatment, we will overcome the current threat posed by SARS-CoV-2 worldwide.

References

- 1 WHO; Novel Coronavirus Situation Report 22; 11 February 2020
- 2 Public Health England; Total UK COVID-19 Cases Update; accessed 31 March 2020
- 3 Moderna; Moderna's Work on a Potential Vaccine Against COVID-19; accessed 1 April 2020
- 4 University of Oxford; Oxford COVID-19 vaccine programme opens for clinical trial recruitment; 27 March 2020
- 5 POST; UK Vaccine Capacity; August 2008



material of SARS-CoV-2 early on and sharing this with the rest of the world. There has also been much investment made in developing vaccines for coronaviruses – a reflection of the fact that respiratory illnesses are generally considered to pose the greatest pandemic risk.

Thirty-five research institutions and pharmaceutical companies worldwide are pursuing a vaccine; some with candidates that have entered animal trials, whilst one, produced by the Boston biotechnology company, Moderna, has entered trials in humans³. Another project at the University of Oxford's Jenner Institute, funded in part by the

been inactivated by passage through a foreign host. These have the advantage of quickly conferring immunity to the person being vaccinated and are a low-cost option, so attractive to governments considering the cost of vaccinating of the entire population at once. Another more modern approach includes constructing a recombinant vaccine that involves the extraction of the genetic code for one of the surface proteins on the virus – the part most likely to invoke an immune response – and inserting it into a bacterium which will then produce large quantities of these proteins which are then manufactured

manufacture is often specific to a particular vaccine and the production facilities are not large enough to produce the supply needed in a pandemic situation. Already, the Coalition for Epidemic Preparedness Innovations (CEPI) is calling for financing to ensure that if and when a vaccine is developed in the relatively near future, there is capacity to produce enough to be of use. Previously concerns have been raised about the UK's capacity to manufacture vaccines on a large scale⁵. It is evident that any shortage of production sites will be felt more acutely in a pandemic situation when all countries are also moving to