COLLABORATION BETWEEN HUMAN AND VETERINARY MEDICINE WILL BE IMPORTANT IN TACKLING ANY FUTURE PANDEMIC DISEASE THREATS

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The current COVID-19 pandemic has reminded us all of the threat to humanity posed by zoonotic infections, that is those that can pass from animals into humans. These diseases make up 75% of the recent infections in humans and it is only a matter of time before the next zoonotic threat emerges. Indeed, it is reported that "there are over 150 zoonotic diseases worldwide, which are transmitted to humans by both wild and domestic animal populations, 13 of which are responsible for 2.2 million deaths per year". In recent years we have observed the global threat from zoonotic coronaviruses such as Severe Acute Respiratory Syndrome (SARS) which emerged in 2002, then 10 years later in 2012 the threat from Middle East Respiratory Syndrome (MERS) and just seven years after this the emergence of Coronavirus Disease in 2019 (COVID-19). Furthermore, as our population expands, the contact between human and wild animal habitats increases, introducing the risk of exposure to new viruses, bacteria and other disease-causing pathogens and thus the risk from future zoonotic diseases cannot be ignored. With this in mind we need to give some careful consideration to the lessons that we can learn from the recent coronavirus infections, including their control and how we can prepare for any future pandemic threats. In doing so we need to reflect on the contribution to our knowledge derived from both human and veterinary medicine.

It is important that information gained from veterinary vaccines should be recognised as part of a One Health approach to medicine, which has been defined as "the integration effort of multiple disciplines working locally, nationally and globally to attaining optimal health for people, animals and the environment". In this regard vaccination has a key role to play within this One Health agenda since it enables us to control disease transmission between animals and human, and in doing so have a significant impact on their shared environments. As a prophylactic measure vaccine can prevent the emergence of disease in the first place and as an intervention they can restrict its transmission and spread within a population. Indeed, several current veterinary vaccines are targeted towards livestock and companion animals and in order to prevent the disease in both animals and humans (for example avian influenza, bovine leptospirosis, rabies and Rift Valley Fever).

As we considered the possibility of tackling the SARS-CoV-2 virus, which causes COVID-19, back in early 2020 something that we did already know from veterinary science was that vaccines against coronavirus infections had been successfully developed over a number of years for livestock (cattle, pigs and poultry) and companion animals (cats and dogs) using both killed (inactivated) and live (attenuated) vaccine strategies. In addition, both Nucleic Acid vaccines based on DNA (similar to the Pfizer and Moderna mRNA vaccines) and Viral Vector Vaccines (similar to the AstraZeneca and Janssen adenovirus vectored vaccines) had both been successfully commercialised for many years against number of veterinary diseases. In fact, a range of viral vector vaccines have been available for multiple animal species since the 1990s and the first ever commercial DNA vaccine was developed in 2005 against a viral disease in salmon and in the same year another DNA vaccine was developed for horses. In addition to veterinary coronavirus vaccines being available, we also knew from veterinary medicine that the coronavirus spike protein was important in eliciting protective

immunity against infection and that virus neutralising antibodies could protect against a virulent disease challenge. Other lessons from animal coronavirus vaccines, that may well have an impact on future COVID-19 vaccine strategies, are protection can be provided by local mucosal responses to topical vaccination via a nasal route, protection can be passed on to offspring from a mother via maternal antibodies, inactivated coronavirus vaccines can elicit at least 12 months protective immunity against a controlled experimental virus challenge and that it is possible to broaden the anti-virus responses to viral variants by combining different virus strains within the same vaccine or by using a prime-boost strategy using different vaccine strains.

Having said this, we cannot fail to be impressed by the exceptional rapid response to the COVID-19 pandemic through the development and deployment of highly effective vaccines within 1 year of the virus genetic code being made available by researchers in China. However, we must be careful not to get too carried away by this success since human vaccines typically take much longer to develop, 10 to 15 years, and the circumstances surrounding this disease may not apply to all future pandemic threats. For example, we knew the vaccine target from previous work on coronaviruses, we had the genetic sequence available and we had vaccine delivery platforms ready to go as a result of years of scientific research. Indeed, the UK Vaccine Network established in 2015 had foreseen the risk posed by such zoonotic infections and had laid the groundwork for a response by funding vaccine platform technologies, developing vaccine process roadmaps and recommending the need for further vaccine manufacturing capability. This should in no way detract us from recognising the heroic efforts of all those involved in developing the COVID-19 vaccines in such a short timeframe and the insightful work of the UK Vaccines Taskforce in managing their sourcing and deployment. As the pandemic develops, we must recognise that there is now a growing need for new and improved vaccine technology platforms offering the opportunity for rapid product development, convenience of manufacture and ease of administration for future disease threats. In order to achieve this, we should utilize existing expertise on veterinary vaccines to evaluate target vaccine antigens in non-rodent animal species, which can often provide better disease models that can more closely mimic the disease in humans, and we should consider shortening the cycle from research to commercialization of human products by validating zoonotic disease vaccines within a relevant veterinary host species. Indeed, it is interesting to note that veterinary vaccines can generally be developed more rapidly than their human equivalents since researchers are able to test the efficacy of experimental formulations in the target animal species using controlled laboratory challenge studies at an early stage in their development. This approach is generally not considered to be ethically acceptable in humans until more is known about the effects of a new disease and its control, although it is interesting to note that the first human challenge studies with COVID-19 have now been approved within the UK. The trials will initially monitor up to 90 healthy 18- to 30-year-olds, who are at low risk of developing complications, after they are given the virus in a safe and controlled environment.

Another risk posed by COVID-19 is its ability to be transmitted from humans back into animals, a phenomenon known as Reverse Zoonosis or Zooanthroponosis. To date this has been known to occur in wild cats, domestic cats, dogs, ferrets, mink and primates. Furthermore, in the case of mink the virus has been shown to be capable of transmission back into humans. Following infection of these contact animals, experimental investigations have revealed that the virus has the ability to mutate in some cases and the potential to cause significant respiratory disease. As a result, vaccines are currently being developed for companion animals and endangered zoo species and animal vaccination is already being selectively rolled out in Russia. Whilst there is no immediate cause for alarm, this situation will require careful monitoring by veterinary scientists in the future if we are to fully understand and control these potential reservoirs of infection.

In conclusion, it is becoming increasingly evident that we should adopt a One Health approach to disease control in the future since it is clear that the health of humans is irrevocably linked to the health of animals and the environment in which they both co-exist. Thus, collaboration between animal and human health researchers offers the potential to advance the understanding of mutually relevant diseases and expand the translational approach to medicine. The World Health Organisation believe that we can achieve this by "designing and implementing programmes, policies, legislation and research in which multiple sectors communicate and work together to produce better public health outcomes". Utilising more relevant in vivo animal disease models and experience with veterinary vaccines can help to accelerate pre-clinical research for human vaccines, and thus shorten the cycle from research to commercialization by validating zoonotic diseases within animals. Any future pandemic preparedness strategy must recognise this and ensure that there is a close collaboration between human and veterinary medicine in the development of any research programme. □