

Securing our future

The value of veterinary vaccines



About this report

This report was commissioned and funded by the British Society for Immunology and the International Veterinary Vaccinology Network.



The British Society for Immunology is the leading UK membership organisation working with scientists and clinicians from academia and industry to forward immunology research and application around the world. Our friendly, accessible community consists of more than 4,200 immunologists, giving us a powerful voice to advocate for immunological science and health for the benefit of society.



International
Veterinary Vaccinology
Network

The International Veterinary Vaccinology Network is an international community of over 1,500 members working together to develop improved vaccines for livestock and zoonotic diseases. The Network provides the opportunity to establish multi-partnered, international collaborations that bring together the diverse skills that can accelerate the development of vaccines for animal diseases that have significant impacts on societies in low- and middle-income countries (LMICs).

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What is a vaccine?

Vaccines are protective treatments that prevent disease by training the immune system to recognise and respond to infectious pathogens such as bacteria, viruses and parasites to stop humans and animals getting sick. This protection can be short-lived or life-long, depending on the type of vaccine and the disease. Some vaccines contain weakened (attenuated) or inactivated versions of infectious agents, particularly viruses. Others contain molecules that mimic specific components of pathogens or toxins produced by bacterial infections.



Investing in veterinary vaccines

The field of vaccine research has received unprecedented attention over the past year. Beyond the recent focus on human vaccines, animal vaccination plays a vital role in protecting UK and global health, wealth, and security. Progress in veterinary vaccinology has underpinned significant advances in vaccines for animals and humans, including in response to the COVID-19 pandemic.

Infectious diseases in livestock and wild animals pose a significant risk to food security and human health, both within the UK and beyond our borders, with new threats continually emerging. Worldwide, the cost of tackling these diseases adds up to many billions of dollars every year, with a disproportionate burden falling on low- and middle-income countries.

The UK has a rich legacy of cutting-edge veterinary vaccinology research, supported by our innovative biotechnology industry and leading role in global vaccine research networks. Not only has this led to the development of animal vaccines that have been deployed all over the world, but it has also underpinned work on human vaccines for COVID-19 and other diseases.

However, our world-leading position is threatened by a lack of strategic long-term investment in the research, skills, collaborations and infrastructure that are necessary to develop, commercialise and manufacture animal vaccines within the UK.

- **We will unlock significant economic benefits for the UK**, by improving the efficiency of farming, reducing the burden of livestock lost to disease, and protecting against future outbreaks.
- **We urgently need to secure the future of funding for all aspects of veterinary vaccinology**, from fundamental immunology and biosecure research facilities through to the development and testing of novel vaccine technologies.

- **We need to see investment in UK veterinary vaccine manufacturing capabilities** in line with the recently established Vaccines Manufacturing and Innovation Centre (VMIC) for human vaccines.
- **We must support career development and opportunities for early career researchers**, in order to build the future veterinary vaccine research workforce.
- **We must prioritise a One Health approach**, fostering close collaboration between human and veterinary medicine and investing in the development of effective, affordable and accessible animal vaccines that will protect against today's diseases and those that are yet to emerge.
- **We cannot do this alone**: we must work with academic and industry partners and support global collaborative initiatives to help protect human and animal health worldwide.

The COVID-19 pandemic has taught us that the UK cannot afford to ignore the threat from infectious disease, especially from zoonotic diseases that jump from animals to humans, and that the health and wellbeing of humans and animals are intertwined. By investing in veterinary vaccine research today, we will be better prepared to respond to emerging threats in the future.

A history of success

The UK has played a leading role in vaccine development in humans and animals for more than 200 years. There are many exciting examples of successful UK veterinary vaccines used in pets and livestock worldwide, playing a key role in improving animal welfare, defending food supplies, safeguarding economies, and protecting human health.



Livestock, pets and wild animals are susceptible to a wide array of infectious diseases caused by pathogens, including viruses, bacteria, fungi, and parasites. Vaccines are a proven way to prevent infectious diseases in animals and a cost-effective way to enhance animal welfare, safeguard food supplies and protect human health, particularly for conditions with limited treatment options.

Many successful veterinary vaccines have been developed in the UK thanks to our experienced research base, a wealth of technical know-how, global positioning, engagement from UK and international funding bodies, and robust bioscience research ecosystem, including world-class sequencing and genomics facilities.

In the UK, veterinary vaccines help control a range of diseases that are endemic in the country, such as salmonella and tetanus, and keep out those that are not commonly found here, for instance rabies and bluetongue. Vaccines can also help control outbreaks of highly infectious exotic diseases, such as foot-and-mouth, which can decimate agriculture with devastating impacts on the local food supplies and economy.

Vaccination also plays a central role in increasing the productivity and efficiency of farming, boosting yields and reducing costs. For example, UK vaccines are widely used to prevent common diseases in farmed salmon and trout, increasing productivity while supporting the fight against antibiotic resistance (see page 11).

Animal vaccines also play a direct role in protecting human health, whether from direct infection from live animals or by combating food-borne pathogens. Examples include salmonella vaccination for chickens, which has significantly reduced food poisoning in humans.

In some cases, vaccines can even help eradicate disease altogether. While public health experts champion the eradication of smallpox in humans, our greatest success in animals has been the elimination of rinderpest in 2011 following the development of a vaccine by British scientists. This has saved countless lives and boosted the agricultural economies of some of the world's poorest nations, saving African countries US\$1 billion annually.

Case Study

Getting rid of rinderpest

Rinderpest or cattle plague affected cattle and buffalo, causing fever, lesions, diarrhoea, and discharge from the eyes and mouth. The virus was spread by air, drinking water or contact with infected animals, and was often fatal. Although rinderpest was well controlled in Europe and the UK by the 1900s using strategies including quarantine, hygiene controls and slaughter of affected animals, outbreaks continued in low- and middle-income countries into the 20th century, killing entire herds and inflicting substantial economic losses and famines affecting millions.

In 1960, Walter Plowright, a British veterinary surgeon and research scientist, developed a simple, affordable, and easily administered vaccine that offered long-lasting immunity to rinderpest in a single shot. The vaccine used a weakened form of the virus produced in tissue culture using similar technology to the human polio vaccine.



Plowright dedicated his career to the eradication of rinderpest. In 1994, the Food and Agriculture Organization of the United Nations launched its Global Rinderpest Eradication Programme (GREP). Thanks to efforts including targeted vaccination programmes, the last known case of rinderpest was recorded in Kenya in 2001. In 2011 it was officially declared eradicated by the World Health Organization, joining smallpox in becoming the only two infectious diseases to be successfully wiped out.

Veterinary vaccinology and immunology also make vital contributions to disease prevention and vaccine development in humans. For instance, basic immunology research in animals including sheep and chickens has underpinned our understanding of immune cell development and migration in humans, providing essential information for developing successful vaccines.

For some diseases, scientists can transfer vaccine knowledge directly from animals to humans. Vaccines against bovine papillomavirus developed in the UK formed the foundations of the human papillomavirus (HPV) vaccines that are now widely used to prevent cervical cancer. Scientists hope that vaccines against respiratory syncytial virus (RSV) can follow a similar path. The vaccines, which have been shown to protect cows, are now entering trials in humans (see page 9).

However, the applications of veterinary vaccine research to human vaccines go beyond individual vaccines. New technology platforms are often developed and tested in animals for veterinary vaccines before being translated to humans, such as the nucleic acid vaccines now being used for COVID-19 (see page 12), and the UK has been a leader in this area.

After two centuries of pioneering work, we have made great progress in the field of veterinary vaccinology. As we face increasing pressure from a growing global population and threats such as climate change and emerging new diseases, it is vital that we build on this momentum to secure our food, economy and health for the future.

The last known
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Leading the world in vaccine research

The fight against infectious diseases is a global one, so we must work internationally if we are to succeed. The UK's expertise in veterinary vaccinology, combined with our global connections, relationships with international funders, and prominent roles in research networks, allows us to engage and empower scientists from around the world to make progress.



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Using networks to pool knowledge

In vaccine research, there are often generic needs that apply across diseases and species, such as the need for effective adjuvants or tests that can distinguish vaccinated and infected animals. However, conventional funding structures mean that researchers often have to compete against each other despite working towards the same goal. As an alternative, creating focused partnerships and collaborations that enable researchers to pool resources and share knowledge can help us maximise our advantages in the fight against our common enemy: infectious disease.

The UK is home to several veterinary vaccine research networks, including the British Society for Immunology Comparative and Veterinary Immunology Group (BSI CVIG), which brings together immunologists working in different species for discussion, collaboration and exchange of ideas. Another is the International Veterinary Vaccinology Network, which brings together researchers working on animal vaccines from around the world and is led by the UK. The UK also plays a leading role in STAR-IDAZ, an international research consortium on animal health and zoonotic diseases.

International networks and the projects they enable can have far-reaching consequences. For example, the ChAdOx viral vaccine vector developed by the Jenner Institute and Oxford University was used in an international project to tackle Rift Valley fever in sheep, goats, and cattle, providing vital safety data before being used in the Oxford AstraZeneca vaccine for COVID-19.

Protecting lives and livelihoods

The UK has traditional connections with many low- and middle-income countries (LMICs), where many people rely on livestock production for much more than just food. Their animals are their livelihood, so the health of their livestock influences their ability to give their children a good education and a safe place to live. However, infectious diseases are a constant threat to these people, their animals and their way of life. People in LMICs are also disproportionately affected by neglected zoonotic diseases that are passed between animals and humans, which can damage their long-term health.



We are a global community. What affects one person in Kenya is important for the population in Angola, in South Africa, in Egypt, in the UK and elsewhere.



Professor George Warimwe, KEMRI-Wellcome Trust Research Programme and the University of Oxford

The UK is a part of many programs aimed at improving animal health in LMICs in collaboration with international funders such as the Bill and Melinda Gates Foundation. For example, the UK leads GalvMed, an Edinburgh-based initiative that makes livestock vaccines, medicines and diagnostics accessible and affordable to the millions of people that rely on animals for a living. The initiative directs several programs to expand access to veterinary vaccines in LMICs and bring new vaccines to market for key diseases affecting these regions.

GalvMed (www.galvmed.org) has supported trials and commercial development of vaccines against porcine cysticercosis, a parasitic disease caused by tapeworms. The tapeworms are passed from pigs to humans through the consumption of raw or undercooked meat and can cause neurological problems, including epilepsy. This project led to the first approved vaccine against the disease to prevent infection and transmission to humans and other pigs.

Empowering scientists around the world

The UK supports initiatives that train and mentor scientists in LMICs, supporting and empowering local researchers. These international networks and programs provide scientists worldwide with mentorship, resources and collaborations with leading researchers that help them tackle problems affecting their communities.

For instance, the Zoonoses and Emerging Livestock Systems (ZELS) initiative funds research programs in the UK and abroad to combat diseases in animals that can spread to humans. They have projects in 11 developing countries involving 19 UK research institutions and 30 overseas institutions. The initiative also provides funding for training doctoral students in the UK and overseas.

Although working to fight disease in LMICs provides clear benefits for the people there, it is not a one-way street. The relationships built through international initiatives and networks enable us to communicate honestly about emerging diseases. Furthermore, working with countries where there are no pre-existing disease surveillance systems provides opportunities to establish ways of monitoring for new threats to humans or animals that could spread around the globe and become a threat to the UK (see page 14).

Case Study



**International
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Network**

Establishing the International Veterinary Vaccinology Network (IVVN)

The BSI is a member of the International Union of Immunological Societies (IUIS), whose veterinary immunology committee has been instrumental in establishing international collaborations. In 2013, at an IUIS workshop, STAR-IDAZ consulted the global research community about gaps in capability in veterinary vaccinology.

“There were some generic gaps in vaccinology research which we thought would benefit from coordinated effort. So we knew we needed to bring the community together,” says Dr Sadhana Sharma, Head of Bioscience for Integrated Understanding of Health at the Biotechnology and Biological Sciences Research Council (BBSRC), which was instrumental in setting up the VWN.

After surveys, workshops and discussion with the community, BBSRC decided to create a community-led network established in 2014, called the Veterinary Vaccinology Network (VWN).

“We brought together the animal health community, which was working on various diseases and species to work together as a joint community and learn from each other,” says Sharma. The network galvanised the community and was so successful that it became the inspiration for other vaccine networks in the UK and the US.

After securing funding through a global challenges research fund, the VWN morphed into the International Veterinary Vaccinology Network (IVVN). The IVVN now has over 1500 members around the globe working on a range of species, diseases and vaccine technologies, and has been instrumental in crucial vaccine research. Beyond its research successes, the network has provided a voice for the community, built leadership and capacity in the UK and abroad, and enhanced our preparedness for combating emerging diseases.

Understanding the immune system underpins vaccine development

Fundamental immunology research lays the foundation for effective vaccine development. However, we know much less about immunity in larger animals than we do in humans or mice, which are commonly used in medical research. What's more, tools and reagents for veterinary immunology research are limited compared to their human and mouse equivalents, limiting the progress of research and slowing vaccine development.

From immune responses to better vaccines

Vaccines work by exposing an animal to a substance called an antigen that stimulates a protective immune response to a harmful pathogen, such as a virus or bacteria, without causing the disease itself.

We can identify what makes a good protective immune response by looking at animals who have survived a disease and investigating the biological pathways that are protecting them. For example, are specific antibodies required for immunity, or does a particular type of immune cell need to be activated? Once we have this knowledge, we can engineer vaccines that stimulate an appropriate immune response that will provide effective protection against the disease.

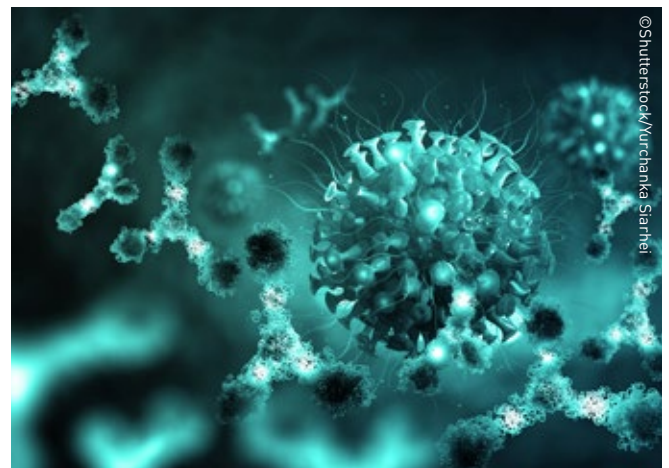
Understanding immune responses can also tell us how to improve our existing vaccines. For example, foot-and-mouth virus vaccines induce immunity to the disease in cattle, but the immunity is very short-lived compared to a natural infection. A more detailed understanding of how immunity develops against the virus that causes foot-and-mouth disease would aid the development of longer-lasting vaccines, which would be a great benefit in countries where the disease is widespread (see page 17).

Another approach to improve vaccine efficacy is to compare immune responses between species. As an example, the foot-and-mouth disease virus infects buffalo, cattle, and pigs, but while buffalo experience few symptoms and cattle are mildly affected, pigs often develop severe disease. Comparing and understanding how the virus interacts with the

immune systems of these different animals could lead to the development of more effective vaccines that stimulate the best response to prevent severe disease.

State-of-the-art technologies, tools and reagents are now opening new doors for understanding disease and immunity. For example, in-depth DNA sequencing and molecular analysis can precisely catalogue the specific immune cells and antibodies involved in the immune response to vaccines and pathogens. And genetically modified cells and animals can help us understand more than ever before about disease and immunity in a wide range of species.

We can also use our knowledge of how viruses attack animals to design new approaches to protect against disease. For example, recent research at the University of Edinburgh's Roslin Institute used gene editing to remove a small section of DNA in pigs that enables the Porcine Reproductive and Respiratory Syndrome virus to enter their cells, rendering them resistant to this deadly disease. In another study, scientists at the Pirbright Institute genetically modified mosquitoes to make them resistant to infection with the chikungunya virus, with the aim of stopping the insects from spreading the disease to animals and humans living in tropical and subtropical regions.



Case Study

Opening the Immunological Toolbox



A lack of laboratory reagents, such as cells and antibodies, often holds back veterinary immunology research compared with human and mouse studies. “Reagents are a suite of tools that allow us to ask what the cells look like, what their functions are and how they act as part of the immune response. So a tool in the Toolbox could be an antibody that allows us to detect a molecule on the surface of a cell, or a protein that allows us to detect secreted products, for example,” explains Professor Jayne Hope from the Roslin Institute.

The UK Immunological Toolbox (www.immunologicaltoolbox.co.uk) is a BBSRC-funded initiative designed to provide a repository of reagents and resources for veterinary immunology research. The global need for a specific Veterinary Immunological Toolbox has been discussed at every IUIS Toolkit Workshop and is run by The Pirbright Institute and The Roslin Institute.

“The Toolbox was created with a view to being able to describe the features of the immune response across a range of animals. We do that by creating new reagents and testing and cataloguing existing ones,” Hope says. The reagents in the Toolbox are all listed on the Toolbox website, where researchers can search for and request the tools they need.

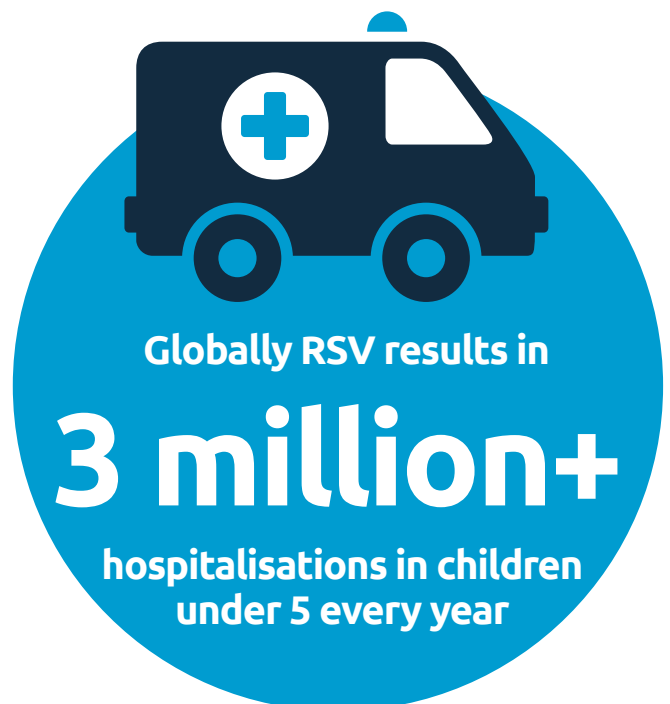
Antibodies form a significant part of the Toolbox, and the team at Pirbright make sure they are permanently secured for future research. “We get the DNA sequence of the gene encoding a specific antibody from the cells that produce it, because once you’ve got that sequence you can always make the same antibody again in the lab,” says Professor John Hammond from The Pirbright Institute. “Sequencing also allows antibodies to be genetically engineered so we can change their species specificity or alter their function and start to ask really detailed questions about how they work.”

From animals to humans

As well as informing the development of veterinary vaccines, a comparative immunology approach can inform human vaccine development. Mice are typically used in early clinical research, but the immune systems of larger animals are often more closely related to our own. Although studies in large animals are more expensive and require specialised facilities, the costs can be offset by a greater chance of success in humans.

Research into coronaviruses in animals highlighted the fact that antibodies and cellular responses are both critical for building protective immunity. The work suggested that there would be a clear benefit in developing COVID-19 vaccines that generate both antibody and cell responses, informing the development of today’s life-saving vaccines.

When human and animal diseases are closely related, vaccine research in animals can be directly translated into humans. For example, the bovine version of Respiratory Syncytial Virus (RSV) is similar to the virus that infects humans, causing severe lung infections in calves and human babies, respectively. Human RSV is a leading cause of hospitalisations of infants under the age of one in the UK. Following extensive studies into the immune response of cattle to the virus, scientists were able to design a vaccine using a structurally engineered viral protein that protected 80% of calves from infection. The knowledge gained from the work in calves is now being applied to human research, and a vaccine based on these insights is currently in human clinical trials.



Safe food for all

The global population is expected to reach more than 9 billion by the year 2050. To meet the demand for food, global meat production will need to increase from 318 million tons in 2016 to 455 million tons by 2050 while also improving efficiency to mitigate the impact on the climate. Veterinary vaccines have a vital role to play in ensuring safe, sustainable food for everyone.

People around the world rely on local livestock for food, particularly in low- and middle-income countries (LMICs). However, infectious diseases are estimated to reduce livestock productivity by around 20%, increasing the cost and reducing the availability of food, leaving already impoverished people to go hungry. Veterinary vaccines increase farming efficiency and reduce losses to disease, improving the environmental impact of livestock farming and helping to provide safe food for everyone over the decades to come.



Global meat production of
455 million
tons per year needed by 2050

Better vaccines for widespread use

For livestock producers to use vaccines to protect their animals, the vaccines must be safe, efficacious, cost-effective and easy to administer on a large scale. Although many commercial vaccines are available, they often fall short in at least one of these areas. This makes them unattractive or unobtainable for many livestock producers, particularly in LMICs.

Many vaccines are expensive, so many farmers do not see them as a cost-effective solution. We must therefore continue to drive down manufacturing costs and make vaccinating animals a cost-effective alternative to medications and losing animals to disease. Furthermore, injecting individual animals is often difficult, particularly in large flocks of smaller animals such as birds.

Current research is focused on the development of multivalent vaccines, which provide protection against several diseases in one dose. There are also innovations in vaccine administration routes, such as in feed, water or as a mass spray. Ease of use and accessibility are also hampered by vaccines that require careful handling and continuous cold storage (cold chains),

which is difficult or impossible in many of the countries that need them most, so work is ongoing to improve vaccine stability.

For some veterinary diseases that threaten livestock, such as African swine fever, there is simply no commercially-available vaccine yet that induces a protective immune response. For other vaccines, such as those against infectious bovine rhinotracheitis, the immunity they provide is short-lived and frequent boosters are required. Furthermore, some vaccines do not provide adequate protection against all strains of a pathogen, as is the case for vaccines against avian flu, bluetongue, and swine influenza - all diseases that can quickly devastate food supplies.

Scientific research and innovation could overcome many of the current problems in vaccine availability, administration and efficacy (see page 12), but progress in these areas is dependent on funding.



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Stopping the spread of foodborne diseases

Estimates from the World Health Organization suggest that one in 10 people fall ill with a foodborne disease each year. Livestock often carry and spread pathogens that cause foodborne illnesses without suffering symptoms themselves, but vaccination can help stop the spread.

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Sometimes people ask why it is so important to protect cattle and pigs and poultry, but it's not only about health and welfare of animals, it's about food production and food security. It's all about food supply to improve the health and welfare of people.

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Professor Bryan Charleston, Pirbright Institute

For example, poultry carrying Salmonella bacteria often have no symptoms but can pass the bugs on to humans where they cause vomiting and diarrhoea. In the 1990s, human cases of salmonella in the UK were increasing rapidly, so scientists developed a new vaccine for use in poultry. The vaccination campaign that followed reduced instances of food poisoning and helped end the salmonella epidemic in the UK.

Despite the success of salmonella vaccines in the UK, many more foodborne diseases can be caught by eating infected animal products. Most of them are caused by pathogens that we do not have vaccines for yet, including bacterial diseases like campylobacter and a range of parasites.

Tackling antibiotic and chemical use in farming

Intensive farming involves keeping large numbers of animals in close proximity, creating ideal conditions for infectious diseases to spread. As a result, agricultural industries around the globe use vast amounts of antibiotics to control infectious diseases. Global antibiotic consumption by livestock was estimated to be over 90,000 tons in 2017 - a figure that is expected to continue to rise over the years to come.

However, every time an antibiotic is used there is a risk of driving antibiotic resistance, which is now one of the leading global threats to human and animal health.

Prudent use of antibiotics can help reduce antibiotic resistance where necessary, but vaccines present a straightforward alternative for preventing and controlling infectious diseases in livestock. Studies have shown that vaccines can reduce antibiotic use on farms by directly preventing bacterial disease and reducing secondary infections.

Case Study



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Tackling tuberculosis in cattle

Bovine tuberculosis (TB) is a respiratory disease affecting cattle, spread by wild badgers. Attempts to control TB have cost the UK over £500 million over the past decade and more than 30,000 infected cattle are currently slaughtered each year following outbreaks of the disease.

The human BCG vaccine can provide some protection against TB in cattle, reducing infections by around 60%. But because the vaccine is based on weakened bovine tuberculosis bacteria, it is impossible to tell the difference between an animal that has naturally been infected with TB and one that has been vaccinated. As a result, vaccinating cattle with the BCG vaccine is currently illegal.

After 20 years of work, collaborations between the Animal and Plant Health Agency (APHA), Aberystwyth University, the University of Surrey and international partners have developed cattle BCG vaccines that can be used in combination with new skin tests that can distinguish infected and vaccinated animals, known as Discriminating Infected from Vaccinated Animals (DIVA).

DIVA tests are similar to existing testing methods but only give a positive result in naturally infected cattle. Early-stage field trials testing the safety and specificity of the DIVA test will be completed this year, with trials combining the vaccine and test following in 2022-2024, with the hope that the combination will help reduce the impact of the disease.

Fresh ideas: Innovation & Industry

Despite the many successes and obvious advantages of veterinary vaccinations, they can be complicated to develop and challenging to improve. For veterinary vaccines to be widely used in agriculture and play their role in protecting food supplies, we need vaccines that are effective, easy to use and safe for animals and humans. New technologies and platforms can help us meet these demands, but we need continued investment in veterinary vaccine research to make this happen.

The birthplace of new vaccine technologies

Many new vaccine technologies were first developed in the veterinary space. This includes platforms that are now in widespread use in humans in the fight against COVID-19, such as viral vector and nucleic acid vaccines, which deliver genetic instructions to cells to make antigens that trigger a protective immune response.

The first nucleic acid vaccine based on DNA to be approved was developed in fish back in 2005, to protect against Infectious Hematopoietic Necrosis (IHN) virus in salmon. The technology was then used in several more animal vaccines and experimental human vaccines against Zika virus, influenza and HIV, before finding rapid success in the form of RNA-based vaccines for COVID-19.

Vector vaccines are based on modified viruses, and were also developed in the veterinary vaccine sphere before being transferred to humans. In the 1990s, viral vector vaccines were developed against various diseases in animals, including rabies, feline leukaemia and equine influenza. The technology was first approved for use in humans against Ebola vaccines, and forms the basis of a number of different COVID-19 vaccines.

Viral vector technology can also be used to create vaccines against two or more different pathogens, providing broad-spectrum protection and increasing ease of use. This strategy is already used in vaccines to protect rabbits against both myxomatosis and hemorrhagic disease. Ongoing research at the Pirbright Institute is now combining viral vector and nucleic acid vaccine technologies with new gene-editing techniques to develop vaccines that prevent multiple diseases in a single shot.

UK veterinary research was also the birthplace of plant-produced vaccines, which are now used to protect against Newcastle disease in birds. We are also leading the way on the use of immune-stimulating complexes (ISCOM), which are a way of packaging up the components of a vaccine in order to increase immune responses and boost efficacy. ISCOMs are currently used in vaccines against equine influenza and are



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The pipeline is looking very strong at the moment because there are things we can do now that we couldn't do five years ago.”

Professor Bryan Charleston, Pirbright Institute

Leveraging advances in biotechnology

Advances in biotechnology and tools like next-generation DNA sequencing, synthetic biology, systems biology, and gene editing provide a robust foundation for research into new and improved vaccine platforms. One example of the effects of new technologies on vaccine development is the advance in cryo-scanning electron microscopy by 2017 Nobel prize winner Richard Henderson from the MRC Laboratory of Molecular Biology in Cambridge. This provided the atomic-level structural information required for the development of new foot-and-mouth disease vaccines (see page 17).

In another example of the power of new technologies, scientists at the Wellcome Sanger Institute used cutting-edge DNA sequencing technology to accelerate the development of a vaccine against a parasite called

Case Study

Improving vaccines for aquaculture



Fish are an important food source, making a significant contribution to economies around the world. The global aquaculture industry suffers from significant losses from disease, impacting fish welfare, public perception, productivity and profit.

"Vaccines have been very successful in preventing disease in fish, and we've seen a dramatic decrease in the use of antibiotics because of that," says Dr Kim Thompson, who

heads the Aquaculture Research Group at the Moredun Research Institute. "But most of the available commercial vaccines are for higher value costly species like salmon and trout."

"Tilapia, for example, is the biggest aquaculture species globally, after carp. It's a very rapidly growing species, so it's a good source of food and revenue for low-income families. However, intensive culture can result in considerable disease problems and fewer commercial vaccines are available for the tilapia compared to Atlantic salmon and Rainbow trout," says Thompson.

Vaccines in aquaculture also have several drawbacks, including the need to vaccinate each fish individually and the fact that the adjuvants used in the vaccines to promote an immune response can have side effects in the fish. "A lot of our ongoing research is looking at different delivery systems that will improve the efficacy of immersion and oral vaccines, new adjuvants for improved safety and cost-effective vaccines for cheaper fish like tilapia," Thompson adds.

Trypanosoma, which is spread by tsetse flies and has a considerable impact on local economies and food security. Until recently, it was thought to be impossible to create a vaccine against Trypanosoma, but researchers were able to identify a target on the surface of the parasite and use it to develop a successful experimental vaccine.

It's not enough to create innovative vaccines - they must reach the market

Although the UK has a strong track record in research underpinning the design and development of new vaccines and innovative technologies, we have been relatively poor at commercialising these advances, especially in comparison to other countries such as the US. This may be partly due to UK funding structures that reward the publication of academic research papers rather than the translation of the ideas within them into commercially viable vaccines or the collaborative work with the pharmaceutical industry that is required to get them to market. Short funding cycles also make it difficult to bring a new vaccine all the way through from initial research to commercialisation, which can require many years of consistent investment.

Fortunately, the UK's leadership and strength in fundamental scientific research are attractive to industry, encouraging inward investment from global companies. But we must encourage further long-term collaborations with industry if we are to bring innovative new vaccines to market.

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We can't ignore the fact that when COVID happened, we were able to respond very quickly because we had technologies available to us such as nucleic acid and vector vaccines because they were developed in veterinary medicine first.

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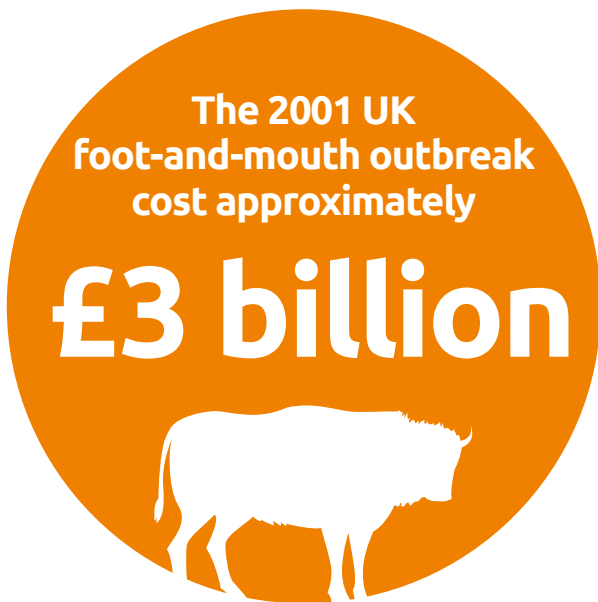
Dr Michael Francis, BioVacc Consulting Ltd

Under pressure: new threats from emerging diseases

The risk from new and returning diseases is relentless. Over the past year, the COVID-19 pandemic has highlighted the devastating impact of new pathogens. But this won't be the last threat we have to face. Intensive farming, changes in human behaviour, global movement and climate change are driving the emergence of new diseases in humans and animals and aiding the spread of existing pathogens that pose a threat to the UK.

The UK is at risk from infectious diseases that threaten animal health

The 2001 UK foot-and-mouth outbreak was a poignant example of the impact of infectious disease, leading to the slaughter of more than six million cows and sheep with an estimated cost of approximately £3 billion. There have been no cases of foot-and-mouth in the UK since 2007, but there is always the threat that the disease will return (see page 17).



Foot-and-mouth is not the only disease that could decimate our agricultural industry if it arrives in the UK. In the face of climate change, vector-borne infections are becoming an increasing concern as warmer temperatures allow midges, mosquitos and other insects to travel further north, bringing diseases such as African horse sickness, Rift Valley fever and West Nile virus. Other threats include peste des petits ruminants, contagious bovine pleuropneumonia and swine fever, which are all spreading rapidly in other countries and could make their way here.

Bluetongue - a viral disease spread by midges that infects sheep, goats, cattle and wild animals including deer - is becoming a significant threat to the UK. The condition causes infertility in animals and can significantly reduce milk productivity, with devastating impacts for farmers. Bluetongue used to be confined to tropical and subtropical regions but has now spread across Europe, with several different versions (known as serotypes) present on the continent. The UK has been free from the disease since 2011, but outbreaks in France and Spain over the past year mean that it may soon arrive on our shores.

There are 29 different bluetongue serotypes, and immunity to one type following vaccination or natural infection does not give immunity to others. Vaccination can prevent bluetongue and was used to control a UK outbreak in 2008, but currently, we only have effective vaccines against a small number of serotypes.

Like humans, animals can also face threats from emerging novel diseases as well as new strains of existing pathogens such as influenza. For example, avian influenza, which is spread by wild birds, is a constant threat to the poultry industry worldwide. There have been several cases of highly pathogenic avian influenza in the UK over the past year, including H5N8 and H1N1, resulting in additional biosecurity measures and the culling of tens of thousands of birds.

“
Infectious diseases can decimate livestock populations, here in the UK as well as the wider world.”

Dr Michael Francis, BioVacc Consulting Ltd



There are viruses circulating in poultry at the moment that haven't yet made the jump into humans and certainly aren't doing human to human transmission, but definitely have the potential to do so.



Professor Fiona Tomley, Royal Veterinary College

Zoonotic disease threats

Controlling diseases in animals is a vital way of reducing the threat of transmission to humans, and vaccines have the potential to make a major contribution. Furthermore, studying these diseases in animals can also give us vital knowledge if they cross into humans.

COVID-19, which likely emerged from a coronavirus in bats, has been a stark reminder of the threat from infections that can jump from animals into humans, known as zoonotic diseases. It is thought that approximately 75% of emerging threats to humans are of animal origin, and MERS, SARS, Ebola, Zika, HIV and the potent H5N1 and H1N1 influenzas are all caused by viruses that originated in animals. In June 2021, there were reports of a person in China infected with a new strain of avian influenza, H10N3. Fortunately, this version is not thought to be highly pathogenic or easily spread, but we may not be so lucky with the next disease that manages to pass from animals into humans.



Case Study



The threat from African swine fever

African swine fever - sometimes called 'pig Ebola' - is a viral disease that affects pigs and wild boar. It causes severe bleeding and is usually fatal. The disease originated in Africa but is now spreading throughout Eastern Europe and Asia in wild boar and domestic pigs, resulting in the deaths of millions of animals worldwide in 2019. There has never been a case of African swine fever in the UK, but as the disease continues to spread, the threat of an outbreak is ever-present, with the potential to cause substantial economic losses in the UK.

The virus behind African swine fever is complex, and immunity to the disease is not well understood. As a result, it has proved challenging to create a safe and effective vaccine. There are currently no commercial vaccines for the disease.

Last year, scientists at the Pirbright Institute announced that they had successfully developed a viral vector vaccine, containing eight genes from the African swine fever virus, that provides 100% protection against severe symptoms of the disease. The vaccine is DIVA compliant (see page 11), so vaccinated pigs can be distinguished from naturally infected pigs - a key component of disease surveillance and containment. More work is needed to bring the vaccine to market, but these early results provide hope that we may be able to fight the disease if it arrives in the UK.

How do we prepare for the next outbreak?

We must be prepared for the next outbreak of infectious disease, whether it is in animals or humans. This relies on surveillance efforts to identify and track threats, flexible vaccine platforms that can easily be adapted to new pathogens (see page 12), leveraging our knowledge and experiences across different species and diseases, and maintaining access to manufacturing capabilities that can produce the vaccines we need in the face of a crisis.

Tracking diseases around the world

Identifying risk is an essential part of the preparation for new and existing disease outbreaks. In the UK, we have advanced surveillance facilities and programs to detect and manage new threats, including the reference laboratories at the Pirbright Institute and the surveillance programs at the Animal & Plant Health Agency.

DNA sequencing initiatives have a central role in tracking how bacteria and viruses are evolving around the world, which may help alert us to the next potential disease outbreak. We must direct these activities to areas where the risk is highest, often in countries with rapidly intensifying farming practices and few local surveillance programs. As a result, outreach and network-building in these countries are vital if we want to see the next threat coming.

To fight emerging diseases, we also need to invest in containment and research facilities here in the UK that will allow us to study and understand new diseases and quickly create interventions to tackle them, including vaccines. Currently, there are only two facilities in the UK with the right level of biosecurity to study highly infectious diseases in animals. This lack of facilities could hamper our efforts to respond to a new outbreak.

Looking to the long-term

We must have the ability to respond rapidly to emerging diseases in humans and animals, through the development of reliable and flexible vaccine platform technologies. Although the success of COVID-19 vaccines may lead people to expect that we can develop vaccines for any new disease in a matter of months, the truth is that developing vaccines against many infectious diseases is much more challenging. Next time we may not be so lucky.

To respond effectively to new outbreaks, we must continue investing in vaccine research and platform technologies that can tackle any disease. Creating new technologies that we can deploy across a range of diseases as needed means prioritising long-term funding into vaccine research and manufacturing, but the current system of short-term funding cycles in the UK makes long-term strategic financing difficult.



We're particularly vulnerable to emerging infectious diseases from animal populations. Unless we consider the risks posed by animals and design control strategies that at least incorporate that knowledge before the next pandemic or smaller scale outbreak, then our control strategies will not be very efficient.



Professor George Warimwe, KEMRI-Wellcome Trust Research Programme and University of Oxford

Bringing knowledge and experience together

When COVID-19 arrived, the UK's vaccine research community was able to respond quickly because of the technology that was already available. This included vaccine platforms that had been developed by veterinary vaccinology researchers over the past decade or more. We also benefited from a wealth of transferable knowledge from creating vaccines for related viruses in cattle, pigs, poultry, dogs and cats.

Case Study

Ready for foot-and-mouth



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Foot-and-mouth disease is caused by a highly infectious virus spread by contact with contaminated equipment, feed or animals. The disease affects cattle, sheep, pigs, goats, and other cloven-hooved animals and usually occurs in low- and middle-income countries, though there have been devastating outbreaks in the UK.

Outbreaks in countries that are usually free of foot-and-mouth cost around US\$1.5 billion per year, while the cost to countries where the disease is endemic is thought to exceed US\$6.5 billion.

Although there were some examples of human and veterinary scientists working together on the COVID-19 response, better communication and collaboration could have further helped to leverage our existing knowledge and experience.

Maintaining an open research community where scientists can exchange knowledge through networks, communities and collaborations will undoubtedly help to accelerate vaccine development, maintain optimal preparedness and respond effectively as a cohesive scientific community in the face of the next threat.

We must increase UK veterinary vaccine manufacturing capabilities

The veterinary vaccine industry has been declining in the UK, and as a result, we have been in danger of losing our manufacturing capabilities. To be able to respond to future threats, we must continue to invest in increasing UK vaccine manufacturing capacity and skills.

The Vaccines Manufacturing and Innovation Centre (VMIC) has now been established to promote and accelerate human vaccine manufacturing in the UK, and the recent announcement of a new Animal Vaccine Manufacturing and Innovation Centre to be established at the Pirbright Institute is welcome, but manufacturing capability is still limited. Increased UK investment in the manufacture of veterinary vaccines would enable us to respond to the new and re-emerging diseases that threaten animals and humans.

“There’s a huge global undersupply of the foot-and-mouth vaccine. It’s one of the biggest selling vaccines in the world, but it’s still not enough,” says Professor Bryan Charleston from the Pirbright Institute, which monitors and researches the disease.

Foot-and-mouth vaccines typically use a ‘dead’ version of the foot-and-mouth disease virus, requiring expensive facilities with high levels of biosecurity to produce them. Adding to the challenge, the vaccine is inherently unstable, reducing its effectiveness.

Scientists at the Pirbright Institute, with collaborators, are developing the next generation of foot-and-mouth vaccines to prepare for future outbreaks. They are using insect cells to produce the outer coat (capsid) of the virus to use as a vaccine, removing the need to use the live virus and reducing the biosecurity demands and cost of production.

“Because we disconnected the capsid production from the virus lifecycle, we were also able to create new bonds that lock the coat structure together,” says Charleston. “Consequently, they induce a much stronger immune response, are more stable, can be stored for longer, and can be adapted quickly for new strains.”

“

When we’re in ‘peacetime’, we need to be investing in surveillance and tools against these infectious diseases so that we’re ready when the next pathogen ‘war’ breaks out.

”

Professor Fiona Tomley, Royal Veterinary College

Growing the next generation of veterinary vaccinologists

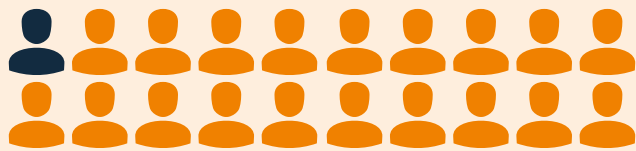
Ongoing vaccine research and development requires a constant supply of bright minds and willing hands. However, few immunologists consider a career in veterinary immunology, and many in the field cite a lack of upcoming talent as one of the biggest barriers to future vaccine development.

Choosing a career in veterinary vaccinology

Researchers entering veterinary vaccinology come from various undergraduate degrees, including biochemistry, biomedical sciences, and veterinary sciences. Most work in veterinary immunology or vaccinology during their masters or PhD before becoming a researcher. However, there seems to be a lack of awareness about the work and impact of research in veterinary vaccines, and a recent survey by the British Society for Immunology (BSI) showed that fewer than one in 20 immunologists would consider a career in veterinary immunology.



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Fewer than

1 in 20

immunologists would consider a career in veterinary immunology

Having an undergraduate degree in veterinary science is not a necessary requirement for working in veterinary vaccinology, and we need to encourage researchers from a broad range of subjects to enter the field. As vaccinology continues to become more interdisciplinary, it demands a wide skillset, from practical biochemistry and immunology to computer modelling and statistics.

Publicity initiatives and campaigns that engage university students and researchers early in their careers and highlight the impact of veterinary vaccine development in food production, disease prevention, human health and animal welfare could also be effective in attracting people into the field. As we've seen in this report, veterinary vaccinology has many exciting stories and challenges to engage the next generation of researchers.

Staying in the field

Once they have begun a career in veterinary vaccinology, we must ensure that there is funding and mentorship available so early career researchers can stick with their chosen path. Unfortunately, postdoctoral positions in veterinary immunology can be hard to obtain, often due to a lack of funding.

In the past, there have been several programs funded by DEFRA, the Wellcome Trust and BBSRC that aimed to bring veterinarians into research. However, these programs lacked the same kind of career progression that is seen in medical research, which has structured integrated academic training programs for clinicians.

“

At the Roslin Institute, we can attract people into PhD positions relatively easily, but we struggle to keep those people moving through the career path to postdocs and early career fellowships. That's partly to do with funding and partly to do with the perception that there's a lack of career opportunities.

Professor Jayne Hope, Roslin Institute

Small grants for postdoctoral and early career researchers, such as those provided by IVN's pump-priming grants, can enable early career researchers to get initial data and industry involvement to support larger grant applications. However, funding is becoming increasingly competitive, and researchers in veterinary immunology can face additional challenges compared with their counterparts working in human immunology. This is partly due to a lack of tools which slow down the pace of research, resulting in lower research productivity and a smaller number of research papers, which are usually the key criteria for the allocation of funding.

Networks and cross-disciplinary collaborations also have a role to play in increasing the talent and diversity in veterinary vaccinology. Reaching out to the broader community can provide resources and skills for veterinary vaccine projects, while demonstrating the impact of veterinary immunology could help attract scientists to the field. Additionally, networks can also help early career researchers find jobs and mentorship that will allow them to continue to advance in their careers.

The lack of funding for early career researchers in veterinary vaccinology often leads them to consider moving to another field or profession with better prospects. Unfortunately, these challenges are not unique to animal vaccine research, and the BSI has found that poor funding and lack of job security are the top two barriers faced by immunologists in the UK. These barriers must be addressed if we want to keep our scientists in veterinary vaccinology and support the next generation of vaccine development.

Case Study



Navigating a career in veterinary vaccinology

Although early career researcher Dr Kate Sutton is from a farming background, she didn't plan to become a veterinary researcher. A master's placement at the Roslin Institute showed her the potential impacts of veterinary vaccine research, so she continued to earn her PhD in chicken immunology followed by two postdoctoral positions, before returning to the Roslin Institute as a research fellow.

She now does fundamental research into chicken immunology, looking at the differences in immune responses between humans and birds. "This helps us design more feasible and robust vaccines for chickens. There are good vaccines out there, but it can be like throwing a dart in the dark because we are basing these vaccines on what we know about human and mouse immune systems, which may not apply to chickens," she explains.

"I hope that someday I will run my own group focusing on the fundamentals of chicken immunology with translational applications in vaccine design," says Sutton. She credits the openness of the veterinary research community with helping her advance through her career despite the challenges. "People want to talk and share reagents and experimental designs - there are lots of people who want to help you."

A One Health approach protects us all

Although human and animal diseases are often considered separate, it is becoming increasingly apparent that the health of people, livestock, wild animals and the environment we share are intrinsically linked. We must work together to tackle the threat of infectious diseases in humans and animals, here in the UK and around the world.

Animal vaccines protect human health

More than 70% of emerging infectious diseases are acquired from animals. We can no longer ignore the connection between human and animal health and the fact that veterinary vaccines are vital for protecting humans and animals alike.

For example, veterinary vaccines play a massive role in ensuring our growing global population has affordable access to safe food. What's more, vaccines designed to combat bacterial infections in livestock help to tackle antimicrobial resistance, which is fast becoming the world's most urgent health threat. Estimates suggest that around 700,000 people per year die from antibiotic-resistant infections, with that number expected to sky-rocket over the next few decades as resistance continues to evolve, in part thanks to the overuse of antibiotics in livestock. Vaccinating dogs against rabies remains the most effective way to prevent disease transmission to humans. Veterinary vaccines can also protect us against new and returning diseases that threaten our safety, security and way of life.

Research in animals aids human vaccine development

Researchers have been using animals as models for human disease research for centuries, and new human vaccines are often tested on animals first. For example, the Oxford AstraZeneca COVID-19 vaccine was tested on pigs before it went into human trials. These tests showed that a booster dose provided enhanced immunity, forming the basis for the two-dose strategy now used in humans. Such studies are only possible thanks to fundamental work into understanding immune responses in pigs and how they translate into humans.

Veterinary vaccine research is often the birthplace of new technologies used in human vaccines (see page 12). Novel vaccines are tested in animals first, providing vital information about their safety and how well they work before moving on to human trials.

For some diseases and species, vaccines developed for animals can be used in humans with few modifications, and vice versa. For example, ongoing work is creating vaccines



against Rift Valley fever that can be used in both humans and animals. Other diseases that have domestic animal hosts and may benefit from cross-species vaccination include Crimean-Congo haemorrhagic fever, Middle East respiratory syndrome (MERs), Q fever, Nipah virus, and Hendra virus. Developing vaccines for humans and animals in collaboration can help make the most of scarce resources, which is particularly important in low- and middle-income countries that are often disproportionately affected by emerging diseases. Furthermore, it's easier for veterinary vaccine scientists than medical researchers to carry out challenge studies, where animals are vaccinated and then infected with a pathogen. These provide valuable data about vaccine efficacy, protection against different variants, and how long immunity lasts.

Bringing a One Health approach to vaccine research

A joined-up One Health approach to disease research and vaccine development enables us to share resources and maximise knowledge and technologies to protect human and animal health. But it's not just about technical solutions. We also need to improve our understanding of infectious diseases and how they operate in different species, as well as discovering how they move between species and how human behaviour and interventions impact disease.

We must continue to invest in projects that integrate different disciplines and stakeholders for a One Health approach to work. A shining example is the work by the One Health

Case Study



Tackling Rift Valley fever in East Africa

“My approach is to recognise the fact that pathogens can move between humans and animals and to leverage knowledge from veterinary vaccinology and use that to benefit human vaccine research and vice versa,” says Professor George Warimwe from the KEMRI-Wellcome Trust Research Programme and the University of Oxford.

Rift Valley fever is a viral disease that affects humans and a range of animals, including cattle, sheep, goats and camels. It is spread by contact with infected blood and animal tissue or by bites from infected mosquitoes.

“This virus affects both humans and animals, so the solutions should not be separate. We need to have more collaboration between medical and veterinary researchers to accelerate the development of vaccines and be more efficient with resources,” he explains.

Warimwe led the development of the ChAdOx Rift Valley Fever vaccine, which uses the same viral vector as the Oxford AstraZeneca COVID-19 vaccine, with the aim of designing a vaccine that could be used in humans as well as animals. Early trials showed that the vaccine gave 100% protection against challenge infections in animals. Results from large scale field trials in livestock in Kenya are expected soon.

A phase I clinical trial in humans is ongoing, and Warimwe credits the One Health approach with speeding up the vaccine development process.



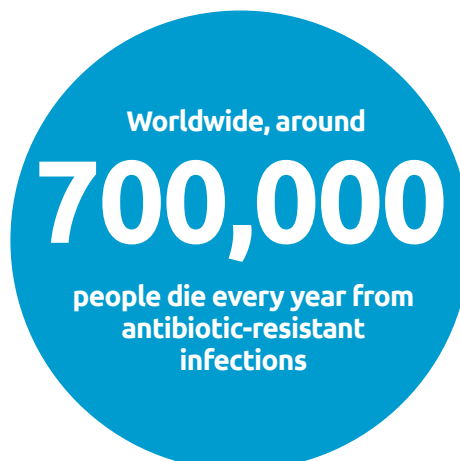
The One Health concept is all about thinking about animal health, human health, human behaviour, and the environment holistically. Implicit in this is the idea that it's not just about sharing technical solutions, it's about integrating disciplines and maximising your advantages.

Professor Fiona Tomley,
Royal Veterinary College



PoultryHub, led by the Royal Veterinary College. The hub's researchers are investigating diseases in poultry in Asia and studying how local systems, farming practices and human behaviour influence the spread of disease and the risk of transmission from animals to humans. However, its work has recently been hampered by a 67% funding cut, highlighting how science and research can be negatively affected by the political priorities of the government of the day.

Tackling the threat of infectious diseases requires investment and collaboration at all levels, from fundamental science to socioeconomic research, together with government bodies including public, environmental and animal health authorities, which currently operate independently. Taking a connected One Health approach to vaccine research helps us identify new threats and leverage our assets to fight against all infectious diseases, wherever they are found.



Fit for the future

The UK has a proven track record of success in veterinary vaccinology, but there is much more that needs to be done. We must build on this legacy by supporting the development, testing and manufacture of new vaccines to secure animal and human health for the future, both at home and abroad.

The COVID-19 pandemic has highlighted the impact of infectious diseases on health and the economy, both on a national and global scale, as well as the risks posed by pathogens that can be transmitted from animals to humans. As the climate changes and the world's population grows and becomes ever more interconnected, we can only expect these threats to increase.

Strategic long-term investment in veterinary vaccine research is not only essential for protecting animal and human health, but will improve farming efficiency and ensure safe food for all. In return, this investment will bring significant economic benefits here in the UK and around the world, particularly in low- and middle-income countries.

The UK is well placed to support the end-to-end journey of vaccine research from bright ideas in the lab through to the development of novel vaccine technologies and platforms, field testing, commercialisation and manufacture. But we cannot do this alone. We have a golden opportunity to secure our position as a global leader in the field by supporting the international networks and collaborations that allow vaccine researchers to pool resources and build relationships with key players around the world, building capacity and expertise where it is needed the most.

“We must bring together the veterinary and medical communities, and invest in the research, technology and infrastructure we need to protect the health and wellbeing of animals and humans everywhere”

Professor Dame Sarah Gilbert,
University of Oxford

“Infectious diseases not only harm livestock, pets and wild animals, but they put our own health, food and livelihoods at risk. We must continue investing in veterinary vaccine research, technologies and manufacturing as well as encouraging uptake of existing vaccines.”

Professor Lord Alexander Trees,
Chair of the ZELS Independent Programme
Advisory Group

It is also vital that we encourage collaborations between academic researchers and industry to increase manufacturing capabilities and bring the commercial know-how that is needed to successfully take new vaccines to market. And we need to do more to bring fresh talent into veterinary vaccinology, support cross-disciplinary working, and enable early-career researchers to thrive within the field.

While the eyes of the world have been fixed on COVID-19, other infectious veterinary diseases have continued to claim countless animal and human lives, especially in poorer countries. Yet we cannot isolate ourselves from these risks. The UK must act to stay ahead of the threats to our own health, economic stability and food security that are posed by existing and as yet unknown animal pathogens. If we want to be ready for what comes next, we must prepare now by building the skills, technologies and capabilities in veterinary vaccine research and manufacture that will enable us to meet the next challenge head on.

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