POLICY FORUM

AGRICULTURE

Unlock the potential of vaccines in food-producing animals

Broader coverage can have economic, climate-related, animal welfare, and human health benefits

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Animal vaccines help maintain healthy livestock and poultry populations, improve food safety, and reduce the transmission of zoonotic disease to humans (*1*). Such vaccines can reduce the clinical impact of pathogens on an individual animal, an important ethical consideration for improving animal welfare. However, the extent of routine vaccination among food-producing animals in low- and middle-income countries (LMICs) is low and considerably lags vaccination rates in high-income countries (HICs) (see fig. S1). Many of the existing gaps in the area of vaccine development and deployment for terrestrial food-producing animals could be hugely aided by changes in policy and increases in funding. But this is also a scientific problem of fundamental importance and applied relevance. Improvement could simultaneously help mitigate climate change and pandemic risk, tackle antimicrobial resistance, and fight poverty. Few global investments could claim to have similarly broad benefits at so modest a cost.

The global livestock and poultry sector plays a critical role in global food production and security and economic well-being, especially among marginalized populations. Furthermore, animal protein is an important source of nutrition for a substantial proportion of the world's human population, and consumption is increasing rapidly. Yet vaccines remain considerably underused in animal health, despite playing a tremendous role in human health. However, although they are currently underused, the deployment of certain vaccines has had a transformative impact on animals. Perhaps the most powerful instance of this is the rinderpest vaccine, which resulted in the eradication of this cattle disease (*2*). Another example is how rapidly the equine West Nile virus (WNV) vaccine was developed after the first identification of WNV in the United States. Although we focus on terrestrial food-producing animals, we recognize the need for developments on vaccines for aquatic animals as well.

ADVANTAGES OF VACCINATION

There are many reasons to support the wider use of vaccines in food-producing animals.

Improving economic well-being

Livestock are a crucial asset and store of wealth for many poor households in the world, particularly in rural areas where agriculture and livestock production are primary sources of income and food security. They play an important role in providing a safety net for poor households and can be used as a source of food and income during times of hardship, such as droughts or economic downturns. However, they are more risk-prone than are other durable assets.

Mortality rates and productivity vary greatly between HICs and LMICs. However, this gap in morbidity and mortality in food-producing animals and productivity can be narrowed with use of vaccines. For example, administration of a live double-deleted bovine viral diarrhea virus (BVDV) vaccine has been found to increase milk production (*3*). According to the Food and Agriculture Organization of the United Nations (FAO), milk yield varies greatly; for example, from Bangladesh and Nigeria the average is 500 kg per animal per year, and in developing countries such as Iran, the average is >2000 kg per animal per year (*4*). Although several factors are responsible for this difference—including breeds and animal nutrition, hygiene, and health—vaccination could help narrow the gap in yields.

Reducing pandemic risk

Rising demand for meat production has led to increased interaction between meat industry workers, veterinarians, and farmers and the livestock animals themselves, including poultry, swine, and cattle. Increased vaccination of domesticated animals can improve herd health and increase immunity to spillovers from wild animals. First, because contacts between humans and terrestrial food-producing animals are high, reducing spillover from wildlife to these populations could avert subsequent transmission to humans and potentially prevent pandemics. Second, protecting domesticated animals from disease through vaccines can reduce consumption of wild meat; such consumption facilitates spillovers. For example, the outbreak of African swine fever in China in 2019 resulted in a shortage of pork, which potentially led to a surge in consumer demand for wildlife as an alternative protein source. Last, vaccination is also crucial to contain the transmission of emerging infectious diseases, especially when their clinical signs resemble those of vaccine-preventable diseases. For example, in regions with low vaccination rates against Newcastle disease, the identification of highly pathogenic avian influenza in chickens is often delayed (*5*).

Although vaccines are important to reduce potential spillover to humans from terrestrial food-producing animals, they are not sufficient, and improving biosecurity in livestock and poultry production requires management measures. These play a strong complementary role in preventing disease spillovers and pandemics.

Mitigating climate and other environmental impacts

The livestock sector is a substantial contributor to greenhouse gas emissions and other environmental impacts, such as land use and water pollution. Recent work has quantitatively shown that greenhouse gas emissions could be reduced by decreasing the burden of animal diseases [for example, (*6*)]. Although the magnitudes of these reductions are likely to be heterogeneous for many underlying reasons, including differences in breeds and production systems that contribute to productivity variations, improvement of animal vaccines could decrease the environmental effects of livestock farming. In particular, wider use of vaccination in conjunction with improved breeding and animal health interventions could allow current levels of outputs of meat and milk to be produced with smaller herds.

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Addressing antibiotic resistance

There is a large body of evidence that animal vaccines can reduce the need for antibiotics in animals raised for human consumption (*7*). In poultry and swine, in which antibiotics are widely used for growth promotion [for example, (*8*) for poultry] and disease prevention, vaccines stimulate the immune system to produce antibodies that can help protect against disease but also reduce the severity of a disease if the bird does become infected, which can also reduce the need for antibiotics. According to a recent expert ranking conducted across multiple countries, vaccines were identified as the most feasible alternative to the use of antimicrobial agents in pig production (*9*). Vaccines cannot replace good biosecurity practices and proper herd or flock management but work as stand-alone interventions to reduce the use of antibiotics.

SCALING UP

Veterinary vaccines offer distinct benefits because they can be developed and licensed more rapidly and cost-effectively as compared with human vaccines (*10*), able to be deployed with trials having a more limited footprint than that of human equivalents. Because safety and efficacy studies are more universally applicable across populations of livestock than they are in humans, licensing processes may be simpler. Moreover, liability considerations related to adverse reactions are substantially lower for manufacturers of veterinary vaccines as compared with those producing human vaccines.

Rapid vaccine development is possible in animals, particularly in response to emergencies, as seen with the equine WNV vaccine. When the disease was discovered in the United States in August 1999, the veterinary vaccine industry collaborated with the US Department of Agriculture Center for Veterinary Biologics to swiftly create an effective vaccine for horses. By August 2001, a conditionally licensed equine vaccine against WNV was available, and today, although not formally required, the WNV vaccine is a core vaccination recommendation for horses in the United States. From basic discovery science to commercialization, a number of key steps must be achieved, including the creation of a target product profile, a discovery and feasibility phase, early-phase development, and late-phase development. Although this global process has some parallels with the pathway to human vaccines, there are some key differences (such as no clinical phases).

Challenges ahead

There are numerous challenges that face the development and deployment of animal vaccines. Crucially, there is currently a dearth in funds for research and development for animal vaccines. In contrast to human vaccination, which is seen as a public good, animal vaccination is often seen as more of a private good for farmers, even if there are broad public goods benefits such as we have outlined. The market for annual vaccines is estimated at beween $8 billion and $12 billion, but available estimates of annual investment into new animal vaccines peg this at less than 1% of this level (*11*). Investment in basic research could lead to the development of new (or next-generation) and effective livestock vaccines against a variety of diseases that affect LMICs, such as East Coast fever and bovine tuberculosis, but also help to address directly climate and antibiotic resistance.

Second, adoption of vaccines by smallholder farmers and marginalized populations is limited by their constrained ability to pay and the lack of focus by the private sector in providing vaccines to this population. There are substantial gaps in the perception of the value of vaccination among farmers. A recent study found that vaccinating against East Coast fever helped reduce livestock mortality, increased milk production, and resulted in savings from decreased antibiotic and acaricide treatments. The study linked animal vaccination to increased household disposable income and higher school attendance by girls in pastoral communities in Kenya (*12*). Similarly, vaccination of chickens against Newcastle disease was shown to increase flock size and improve child nutrition and growth, but perceptions of value, challenges in vaccine delivery at the household level, and ability to pay constrain uptake (*13*). However, farmers' understanding of both the narrow economic benefits to them and broader societal benefits was low. For example, porcine cysticercosis, a zoonotic disease with pigs as a reservoir and caused by a tapeworm (*Taenia solium*), can lead to cysts in the brain, eye, or other tissues of humans, leading to severe consequences


Cows on a farm in Lujan, Argentina, are vaccinated by a veterinarian.

PHOTO: RICARDO CEPPI/GETTY IMAGES

such as epilepsy if humans ingest tapeworm eggs in contaminated food or water. An effective vaccine against porcine cysticercosis now exists commercially but is poorly adopted because farmers are not compensated for the added food safety value provided by vaccinated pigs. We show the benefits of increasing vaccination rates against bovine paratuberculosis both to farmers by increasing milk production and to society by decreasing global carbon emissions (see fig. S2 and supplementary materials).

Third, there are several pathogens that affect food-producing animals, and these vary by livestock or poultry species and by geography. Therefore, scale economies that are possible with the development and manufacture of human vaccines are limited. For some diseases of interest that are common globally—for example, Newcastle disease and classical swine fever—a global vaccination program is more easily scalable. But new vaccines and/or markets would have to be created for vaccines against diseases of interest that are only in LMICs, including peste des petits ruminants, a viral disease that affects sheep and goats; contagious caprine pleuropneumonia, a respiratory disease of cattle; and East Coast fever.

Fourth, many animal diseases encountered in LMICs simply do not have a vaccine. Development of these vaccines—including multivalent vaccines that can confer immunity to multiple diseases and strains, and thermotolerant vaccines that do not require a cold chain—could help to increase access to animal vaccination. This is unlikely to happen without a substantial market for these vaccines or an externally subsidized effort.

Last, even when vaccines are available, vaccination is not always recommended. For some pathogens in certain animals, such as Marek's disease in chickens, vaccines that imperfectly block transmission can lead to the evolution of more virulent strains (*14*). Thus, the rational design of animal vaccines is imperative. Furthermore, trade restrictions have been cited as a reason why many countries do not vaccinate against highly pathogenic avian influenza or against foot and mouth disease (FMD). In both instances, vaccinated animals can still test positive for the disease, potentially affecting export opportunities to countries that are FMD-free and have stringent import regulations. To resolve such issues in the global trading system, countries could agree to adopt a more risk-based approach to trade, being more inclusive of vaccinated and monitored populations.

On a more granular level, specific vaccines could be developed to aid in this venture. In particular, DIVA (differentiating infected from vaccinated animals) vaccines include specific markers or antigens that can be distinguished through diagnostic tests and are increasingly used in animals to differentiate between vaccinated animals and those naturally infected with the pathogen. DIVA vaccines help to prevent the spread of the disease and support disease surveillance efforts by allowing veterinarians to distinguish between vaccinated and infected animals during outbreak investigations.

Manufacturing and delivering

Investing in production capacity for animal vaccines that is more widely distributed could provide "warm" production capacity that can be switched over to a pandemic human vaccine in an emergency. The manufacturing capacity needed for achieving an equitable coverage of livestock around the world would be more than adequate for multiple doses of a human vaccine. Although biosecurity would be a concern for such a facility, these are diminished in the context of mRNA vaccines in which there is no live pathogen involved in the production process, and therefore a facility that makes animal vaccines could be quickly repurposed to make vaccines for humans. Admittedly, animal mRNA vaccines are still only in exploratory stages, and much work remains to be done. Moreover, issues of room-temperature storage of mRNA vaccines and bringing animal vaccine manufacturing to good manufacturing practice standards need to be tackled. But imaginative approaches to leveraging volume production of vaccines for animals and humans could help both sectors.

Delivery of vaccines will also require a substantial rethink of the current model. In India, a National Digital Livestock Mission has been proposed to track the health and vaccination status of livestock, much like with childhood immunizations in the country (*15*). Digital public goods, along with more attractive markets for animal vaccines, could ensure that vaccines reach every village where they are needed.

A PATH FORWARD

To achieve a major revolution in animal vaccination, a number of key measures will be needed. First, a cross-disciplinary approach for rational vaccine development that melds basic and applied research could develop new (and/or next-generation) broadly protective shelf-stable animal vaccines. This will also require a proper measure of vaccinal benefits at the individual level. In tandem, a large-scale monitoring of animal vaccines and their deployment with oversight by the World Organisation for Animal Health along with international partners could provide a quantitative global assessment of their usage, coverage, and population-level effectiveness.

Second, increasing production and deployment of these vaccines on a global scale will require a nimble process for global prequalification, which builds on regional lists of prequalified vaccines, expanded national regulatory capacity, a combination of stakeholders, and a consistent regulatory environment across countries. For example, a prequalification for FMD vaccines exists at the FAO, but this process is not as broad as the prequalification process for human vaccines under the World Health Organization. Among others, these processes will include within-country development as well as multinational organizations such as the European Commission and funding bodies such as the Wellcome Trust. Third, this ambitious undertaking will also hinge on the buy-in of individual farmers in LMICs to vaccinate their animals en masse and government entities to facilitate this process.

Perhaps most importantly, the common thread among these initiatives is a necessity for funding. For human diseases, the $23 billion in financing by Gavi, the Vaccine Alliance since its founding in 2000 was instrumental in scaling up access to childhood vaccines for more than 981 million children in the world's poorest countries and likely prevented more than 16.2 million deaths. Moreover, Gavi's funding has transformed the market for childhood vaccines, helped bring new vaccines to market, and enabled their introduction into national immunization programs. A similar scale of investment of $1 billion a year through a financing entity focused on animal vaccines could transform the marketplace and deliver economic, health, and environmental benefits. ■

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SUPPLEMENTARY MATERIALS

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