

**Letter to Editor**

## **Evidence-Based Approach to One Health Vaccinology**

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Only a few human vaccine trials have been reported from the least developed countries. The target population of biological products often does not have the same opportunity to participate in pre-and post-licensing studies (1). The COVID-19 vaccine trials may have been exceptional. At the same time, in many developing countries, biopharmaceutical research and development have not been pursued with the same vigor as other pharmaceutical industries. For example, despite a century of history of the vaccine industry in a country like Iran, the allocated budget and established infrastructures in the contemporary have not been parallel to other fields of the pharmaceutical industry. On a global scale, the progress of the animal vaccine industry is not comparable to that of humans. A detailed comparative review of human and animal vaccine research methodology revealed that the concepts are not apparent in the animal sector (2). Accordingly, the terminology and assessment of animal vaccines should be standardized and strictly applied. A surveillance system that follows up on vaccines and adverse reaction information is an exemplary human benefit. Although, in many cases, there is no such infrastructure in the animal sector, so it is not possible, to a certain extent, to assess the safety and effectiveness information of approved animal vaccines.

Several studies assessing the quality of vaccine publications have demonstrated this unpleasant reality

that animal studies are lagging in Evidence-based Vaccinology compared to the human side (2-4). Evidence-based decision-making within vaccine research requires a systems approach. To this end, it is necessary to design and carry out studies on vaccines to generalize them in the target communities while having the highest level of external validity. These studies are of more excellent evidential value when conducting randomized intervention studies. However, they should concentrate more on observational studies and post-market surveys at the post-licensing stage (2, 3). In this case, a systematic review resulting from some effectiveness and observational studies may provide more empirical evidence than several Randomized Controlled Trials (RCTs) conducted under controlled and non-generalizable conditions.

The strict RCT protocols and clinical study registration systems that have been grounded in medical science are not a common phenomenon in veterinary clinical sciences in many countries. The clinical trial registration networks should deal with conflicts of interest and prejudice. The centers of the world that manage the knowledge and synthesis of other research are limited in animal health and veterinary medicine. These centers are intended to synthesize research results to generate second-and third-generation knowledge products and facilitate the implementation of the best available evidence.

This issue is essential to developing the new biological product and importing and including vaccines in national immunization programs. The harm caused by the endemic disease can be more significant if the vaccine is selected and used negligently (5, 6). For example, generally importing and administering killed vaccines is merely considered harmless in Iran; the same presumption observed in the national selection of vaccines for Covid-19 in the human population. On the other hand, there are no restrictions on distributing imported live attenuated vaccines or other platforms to certain animal species. Experts have repeatedly warned of the possibility of reverse virulence or abnormal pressure on endemic strains in circulation by heterologous vaccine strains. The absence of an evidence-based decision-making framework in vaccine science will cause irreparable harm.

One issue revisited over the past several years is vaccines' nonspecific (also referred to as heterologous or off-target) effects (5, 6). Vaccines can have beneficial or harmful effects, such as morbidity and mortality, that were not initially targeted. A recent systematic review of the nonspecific effects of vaccines on animal populations has identified a gap in reporting. The presumption attributed this gap to the shift of platforms to the next generation and new technologies, so nonspecific effects had been irrelevant for years. Nevertheless, a systematic review has shown that the evidence in animal populations is scarce and controversial, so nonspecific detrimental or beneficial effects do not appear to be limited to a particular product, platform, or species. The absence of evidence is not evidence of absence (5).

The critical question is how far the nonspecific effects of vaccines, inactivated or otherwise, are likely to impact animal health significantly. Furthermore, what kind of vaccine and immunization schedule will be if that information is available? What if we could conclude that not receiving a specific vaccine is more profitable than using it? For

instance, the vaccinated population is susceptible to other diseases, or their production is reduced, and so on. The surveillance system is needed to monitor the long-term effects of vaccines and vaccinations on the population, the same lack of pain noted above. This information is only helpful if compared and viewed across large populations. Similarly, post-licensing assessments of vaccines should not be limited to immediate or short-term responses following immunization, but detailed monitoring and population studies are required.

Planning for a vaccine as part of a national immunization program should be targeted and evidence-based, with input from other health services. Evidence-based decision-making about vaccines, food, and drugs is an entirely interdisciplinary issue for the nation's health and economy. Therefore, a single yet holistic body should regulate and standardize the overall process. "One Health" entry into vaccines and vaccination to coin the term "One Health Vaccinology" emphasizes the multifaceted and interconnected relationship (7, 8).

One Health means "there is one single health"; an integrated approach to the human, animal, and environmental health, including plants and ecosystems. Implementing integrated health governance will offer a holistic solution to complex problems. It means that sustainable development will not be achieved if One Health does not address the new global challenges. These include emerging and re-emerging diseases, zoonoses, antimicrobial resistance, food security and water sanitation, climate change, and more. The approach engages multiple sectors, disciplines, and communities at diverse community levels, sub-national, national, regional, and global, to foster well-being and address threats to health and ecosystems (7, 8).

The use of vaccine knowledge, economic assessment, and the infrastructure of the parties require access to credible evidence, including safety and cost-effectiveness information. It is only possible through

the evidence-based approach. Alternatively, information on vaccine success and failure within the animal population may not be generalizable to the human population and vice versa.

One-Health Vaccinology requires that vaccine studies be evidence-based. Therefore, Evidence-based Vaccinology provides the framework for One Health Vaccinology. In this context, it is possible to make decisions and implement evidence-based practices in the human and animal sectors and benefit from a healthy ecosystem on a healthy planet. That underlines the urgent need for One Health, the National Committee, to legislate, regulate and evaluate human and animal vaccine studies concurrently. This committee will review vaccine studies and levels of evidence on intervention outcomes. Given that vaccines and vaccinations are interrelated with public health, the economy, and national security, we can only generalize the discoveries to other groups and communities if they are evidence-based. It is unequivocal Evidence-based One Health Vaccinology.

#### Authors' Contribution

Study concept and design: Z. B. S.

Acquisition of data: Z. B. S.

Analysis and interpretation of data: Z. B. S.

Drafting of the manuscript: Z. B. S.

Critical revision of the manuscript for important intellectual content: Z. B. S.

Administrative, technical, and material support: Z. B. S.

#### Conflict of Interest

The authors declare that they have no conflict of interest.

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