

# Role of Immunization and Vaccines for Controlling Bacterial Infections in Animals

Muhammad Qasim<sup>1</sup>, Fatima Amjad<sup>2</sup>, Ijaz Ahmad<sup>1\*</sup>, Amir Iqbal<sup>3</sup>, Muhammad Ibtasam Samijah<sup>1</sup>, Muhammad Touseef<sup>2</sup>, Muhammad Mohsin Zaheer<sup>2</sup>, Waseem Akhtar<sup>4</sup>, Fatima Munir<sup>1</sup> and Rahman Akram<sup>2</sup>

<sup>1</sup>Institute of Microbiology, University of Veterinary and Animal Sciences, Lahore

<sup>2</sup>Institute of Microbiology, University of Agriculture, Faisalabad

<sup>3</sup>Veterinary Officer at Veterinary Research Institute, Lahore

<sup>4</sup>Faculty of Agriculture, University of Agriculture, Faisalabad

\*Corresponding author: [ijazahmaduo6@gmail.com](mailto:ijazahmaduo6@gmail.com)

## Abstract

This chapter describes the significance of vaccines and immunization programs for animals against fatal bacterial diseases. Vaccination and immunization play a vital role in preventing diseases in animals especially in young and pregnant animals which have weak immune system. Vaccination is essential for public health, management of disease and prevention of zoonotic diseases. There are several types of vaccines each vaccine type has its own merits and demerits. It is important that vaccine we used, should meet with the standards of World Organization for Animal Health and the United States Department of Agriculture (USDA). This chapter explores the role of vaccines in stimulating the immune response, minimizing economic losses, reducing antibiotic usage, current challenges and future perspectives of immunization through vaccination. There are still some challenges in developing animal vaccines that include climate change, antigenic variation, complex immune responses, adjuvant, delivery systems, economic considerations, short term immunity, vaccine stability, antibiotic resistance, host specificity of pathogens, which led to stability of pathogens and ultimately diseases objectives of using vaccines and immunization programs in animals. Research in the field of vaccines, using innovative techniques for vaccine development, arranging public awareness programs, help better combating bacterial diseases.

**Keywords:** Vaccines, Bacteria, Vaccination, Immunity, Pathogen

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## Introduction

Bacterial infection in animals causes a wide range of diseases that impact on their growth, health, productivity and welfare (Waters, 2020), from mild to life threatening infections. These infections lead to outbreaks and can spread rapidly in farms, shelters and pets' animals. Common bacterial infections include *Leptospira* in livestock, *Salmonella* in poultry (Shaji et al., 2023), *Brucella* in cattle, and *Chlamydia* in parrots. These infections can show mild to severe symptoms such as fever, lethargy, diarrhea, loss of appetite, and in severe cases, organ failure and even death. Many of these infections can be prevented by following good hygiene practices, biosafety and biosecurity measures and through vaccination (Bloom et al., 2021) and immunization.

Vaccination and immunization play a vital role in preventing diseases in animals (Yadav et al., 2020), especially in young and pregnant animals which have weak immune system. Vaccination and immunization are essential for public health, management of disease and prevention of zoonotic diseases (Dubé et al., 2021). Vaccinating and immunizing domestic and pet animals to prevent zoonotic diseases, and of wild animals to prevent transmission in humans are our main concern (Paul-Pierre, 2009). This step decreases the mortality rate in farms and shelters and increases the productivity of milk, meat and other dairy products. It promotes longer, safer, and healthier ways for domestic and wildlife animals, improving animal and public health and welfare. It also prevents over usage of antibiotics and reduces antibiotic resistance in animals and humans (Micoli et al., 2021).

The objective of publishing this chapter is to enhance the concept of immunization through vaccination, highlighting the importance of vaccines and vaccination programs for better combating bacterial diseases of animal and zoonotic origin, providing awareness related to public health issues caused by lethal bacterial diseases, giving concept of mechanism of action of vaccines and future perspectives for better handling and avoiding outbreaks of bacterial diseases.

## Understanding of Immunization and Vaccination

Immunization is a biological process of protecting the host body from infectious and disease-causing organisms (Sompayrac, 2022), typically through vaccination, by introducing antigen to the body, to stimulate the immune system to recognize and respond to specific

pathogens such as bacteria, viruses, and any foreign particle without causing illness. Principles of immunization is important for designing and developing vaccines (Meyer & Zepp, 2022).

### Principles of Immunization

The vaccine introduces harmless form of disease-causing agent (pathogen), or its part (antigen) into the body. The Immune system of the body identifies the antigen as a foreign particle and responds by producing antibodies, activating other immune cells and creating memory cells (Remembering cells) (Vetter et al., 2018). These cells of the immune system remember the antigen and produce faster and strong response if there is an exposure in the future. If the person is exposed to an actual disease, the immune system can quickly neutralize it due to memory cells. Now, we understand the mechanism of immune response in animals.

### Mechanism of Immune Response in Animals

The immune response in animals is complex and step by step process:

In first step, when pathogens such as bacteria, viruses, parasite enter the body, our immune system identifies this by Pathogen-Associated Molecular Patterns (PAMPs) (Taghavi et al., 2017) present on the surface of pathogen and recognized by immune cells and Receptors like Toll-like Receptors (TLRs) present on the surface of immune cells which detect PAMPs. In next step, Innate immunity quickly produces the physical and chemical barriers (skin, saliva, mucous membranes, stomach acid, and enzymes), Inflammatory Response, and Cellular Defenses e.g., Macrophages and phagocytes (neutrophils), Natural Killer (NK) Cells (Vivier et al., 2008), function as barriers to restrict pathogen entry. In the last step, if pathogen overcomes the innate immune response, it triggers the adaptive immune response.

After engulfing the pathogen, dendritic cells and macrophages represent the antigen on the surface by Major Histocompatibility Complex (MHC) molecules (Monos & Winchester, 2019). This activates the T cells (T Helper cells (CD4+) and T Cytotoxic cells (CD8+). Helper T cells activate the B cells to produce antibodies which bind to specific antigen and destroy it and eliminate it from the body. After the destruction of pathogen, some cells remain in the body and remember the pathogen and make sure to produce faster and stronger response in the future. This mechanism is also induced artificially through vaccines which mimics the natural pathogens but in a complete safe way. Here we discuss the types of vaccines used in animals.

### Types of Vaccines Used in Animals

There are five types of vaccines which are discussed below (Figure 1):

#### Live Attenuated Vaccine

It contains a weakened form of infectious agent (bacteria or viruses) to activate the immune system which can replicate but not cause severe illness. It can provide strong and long-lasting immune response with one or fewer doses. It produces both humoral and cell mediated immunity in animals (Kirimanjeswara et al., 2008). But it is not suitable for immunocompromised patients and those who take immunosuppressant agents. i.e., live attenuated oral polio vaccine (OPV) or Sabin vaccine (Barranco, 2020).

#### Killed/Inactivated Vaccine

This vaccine contains either whole or part of pathogen that is killed or inactivated through heat, chemical and other purification processes, so that it cannot replicate. It is safe for immunocompromised patients. But it cannot provide strong and long-lasting immunity and requires booster doses. i.e., Inactivated Polio vaccine (IPV) (Dubensky Jr et al., 2012). Table 1 describes some bacterial vaccines and type of vaccines used for immunization.

**Table 1:** Classification of some common bacterial vaccines for humans.

Disease or Pathogen	Vaccine type
Plague	Inactivated
Anthrax	Inactivated
Typhoid	Live attenuated
Cholera	Inactivated
Tuberculosis	Live attenuated BCG
Pertussis	Inactivated

#### Subunit/ Conjugate Vaccine

This vaccine contains a part of pathogen and weak antigen with strong carrier protein, sugar and capsid part to induce the strong immune response. It is considered safe because the fragments it contains cannot cause the disease (Vartak & Sucheck, 2016). It produces a stronger immune response in young animals and those with weak immune systems. i.e., *Hemophilus influenza* type b (Hib).

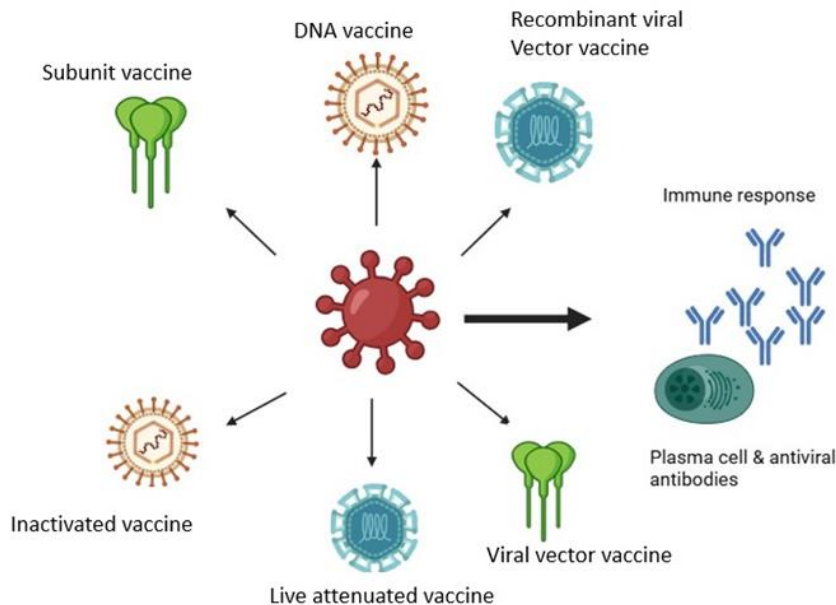
#### Toxoid Vaccine

It contains inactivated toxins (Toxoid) produced by bacteria to stimulate the immune response and cannot cause the disease. It requires booster doses for sustained immunity. It is stable, safe and effective against toxin-mediated diseases. i.e., Tetanus, Diphtheria Vaccine (Angsantikul et al., 2017).

#### DNA and RNA Vaccine

It is a newer technology, containing genetic material with specific antigen that prompts the host cell to produce proteins to trigger

immunity. DNA vaccine transfects specific DNA in the host to stimulate an immune response and RNA vaccine transfects the mRNA (Tombáč et al., 2021) in the host to produce the immunity (Kazakova et al., 2024). These vaccines are safe and have low cost. But these vaccines require cold storage. i.e., COVID 19 mRNA vaccine Pfizer-BioNTech and Moderna and DNA vaccine (Zyduš Cadila).



**Fig. 1:** Different types of vaccines.

### Regulatory and Ethical Considerations in Animal Vaccination

Animal vaccination plays an important and crucial role in prevention and control of diseases and infections (Osterloh, 2022) and in Anti-Microbial Resistance (AMR) (Jansen et al., 2018). So, it is important that vaccine we used, should meet with the standards of World Organization for Animal Health Terrestrial Animal Health Code and authorized by Center for Veterinary Biologics (CVB) (Avram et al., 2023), an agency of the United States Department of Agriculture (USDA). Vaccines undergo preclinical studies, trials, laboratory testing, and trials on animal species to ensure their quality, efficacy and safety (Myhr, 2017). Center for Veterinary Biologics (CVB), an agency of the United States Department of Agriculture (USDA), and Food and Drug Administration (FDA) review these data and findings before giving approval.

In Pakistan, regulatory and ethical considerations in animal vaccination is approved by Drug Regulatory Authority of Pakistan (DRAP) (Malik et al., 2021). Additionally, vaccines must meet the requirements for Good Manufacture Practices (GMP), storage and routine inspection to avoid from contamination and adverse effects. Considering public health and animal safety while using vaccines to prevent zoonotic diseases is also crucial in animal vaccination. Vaccination must be implemented carefully so that animals are not subjected to unnecessary harm while achieving public health safety. In food animals, there must be ethical consideration (Shukla et al., 2024) while using mass vaccines, to prevent from antibiotic resistance and vaccine residues in food products.

### Mechanism of Vaccine Action

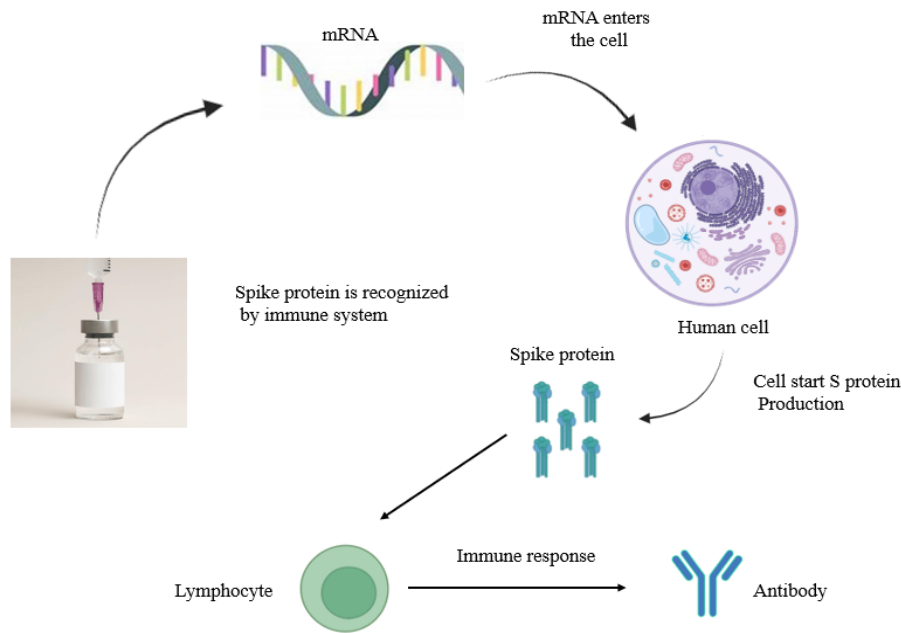
Vaccines containing adjuvants (Zhao et al., 2023) stimulate immune system of the host as vaccine contain the required pathogen against which vaccine has been developed (Iwasaki & Omer, 2020). It depends upon the type of vaccine either it has killed pathogen, live attenuated, subunits or mRNA of the required pathogen. Because vaccine has mimicry with the infectious agent so it can stimulate immune system (Pulendran & Ahmed, 2011) without causing disease in the host. Vaccine has the antigen, part of pathogen and this antigen is recognized by the cells of immune system, so immune system starts its work to degrade antigen. After the administration, the innate system first recognizes, after that, B & T (Swain et al., 2012) cells by creating memory cell's function (Figure 2).

B cells produce antibodies that migrate towards antigen while T cells do not migrate, and antigen associated with MHC molecule (Taylor & Balko, 2022) bind with T cells and Tc cells degrade this complex. Memory cells play a leading role in immunity. When in first encounter, B cells differentiate into two types of cells; Plasma cells that produce antibodies & memory B cells that retain memory for that particular type of antigen. Same is the case with T cells. Memory cells (Raphael et al., 2020) have the ability to produce the same antibodies against that antigen who have already been exposed to the immune system. So, in shorter memory cells produce antibodies and antigen is processed without delaying. Bacterial vaccines activate immune system when innate and adaptive systems recognize that antigen.

### Common Bacterial Infections in Animals

Livestock (Goat, pigs, cattle, sheep etc.) & pets have a variety of bacterial infections in which the causative agents are different, and their mechanism of action is quite different from one another (Prescott et al., 2022). Mastitis, respiratory infections, Foot rot, anthrax, leptospirosis, brucellosis, gastrointestinal tract infections & listeriosis are some common bacterial infections in livestock (Gupta et al., 2017). All these infections required some risk factors, and the symptoms appear may sometimes resemble but to diagnose particular infection, there must be appropriate diagnostic methods which have high sensitivity and specificity. The common bacterial infections of pets include respiratory infections, pyoderma, tick borne diseases, UTIs & gastrointestinal infections (Bhat, 2021). Bacteria through different routes enter the body,

replicate there & can cause localized or systemic infection. Some risk factors like overcrowding and immuno-compromised situation help bacteria to cause infections. These infections have devastating effects on animals' health & cause socio economic loss to the farmers so contributing to the loss of economy of a country (Tiwari et al., 2013).



**Fig. 2:** Mechanism of action of mRNA vaccine.

### Role of Vaccines in Controlling Bacterial Infections

Vaccine plays a crucial role in order to stimulate immune system also in growing ones (Kollmann et al., 2020) to recognize particular antigen from bacteria and if there is exposure of same antigen in the near future, the immune system may not take time to respond against that particular antigen. In a population of animals, when most of the animals are vaccinated there are less chances that a bacterial infection may occur. When we use vaccines to reduce infections, there is surety that less antibiotics are used and for that purpose, antibiotic resistance which is a major issue globally can also be leveled down (Micoli et al., 2021). Brucellosis, a deadly disease of livestock, causes abortion, less milk production and meat loss of animals. Immunization through vaccination has been done & it proves that this mechanism has shown a vital role to remove the brucellosis from a particular form.

Zoonotic bacterial infections that can be transfer by animals to humans can be treated but their prevalence can be stopped (Carpenter et al., 2022) if there is proper use of vaccine if there is the suspect that animals are infected from particular bacterial infections in the form. In case of rabies (Natesan et al., 2023), vaccination is essential to dogs while in terms of brucellosis, the infected animals should be vaccinated, and proper preventive measures should be adapted so that there is less chance of transmission of that disease. Vaccination therefore decreases the risk of outbreak by providing immunity against bacterial diseases. Following Table 2 shows the outbreak of various bacterial diseases in respective year and after mass vaccination the risk remarkably decreases as evident from the statistical data (Swain et al., 2012).

**Table 2:** Efficacy of few childhoods' vaccine in USA

Disease agent	Before vaccination		After Vaccination		
	Number of cases (Year)	Vaccine available (Year)	1997	2002	Decrease in disease incidence
Diphtheria	207,257 (1922)	1942	12	1	>99.9
Pertussis	265,789 (1953)	1952	5589	8298	94
Measles	894,906 (1943)	1963	508	39	>99.9
Mumps	156,890 (1976)	1971	789	267	>99
Rubella	5,978 (1975)	1971	165	18	>99
Poliomyelitis	59,276(1954)	1954	0	0	100
H. influenzae	21,807	1991	-	186	>99

### Impact of Vaccination on Antibiotic Resistance

To combat antibiotic resistance, vaccination is the required procedure (Buchy et al., 2020). When vaccination is done, there is less chance that the disease occurs. So, in that case antibiotics are avoided when the antibiotics aren't used the resistance chances are decreases. Vaccines can also reduce secondary infections, in these types of infections antibiotics are recommended so vaccination process can also overcome the need of broad term antibiotics for such diseases. The link between vaccine and antibiotic-resistant (Rosini et al., 2020) strains is that how vaccine can prevent the resistance. Along with this concept that vaccines can lower the need of antibiotics, vaccine can also play role to minimize

the spread of resistant strain to other animals as well as to humans. The vulnerable populations must require the vaccination procedure in order to have the healthy stage so that if somehow a pathogen attack, the members of that population have the strong immune response against that pathogen and the response time may not be delayed and immediately the pathogen must be killed.

Vaccines target specific pathogen; vaccines can reduce the ration of primary and secondary infections and along with these vaccines can decrease the need of antibiotics. Vaccines can reduce the risk associated with a particular pathogen & may overcome the severity of that disease. Vaccines reduce the time of infection so when the infection time is less there is no need of antibiotics after vaccinating the patient. Vaccination helps in developing antibiotic steward (Mullins et al., 2023) programs. All these strategies help to reduce the use of antimicrobials like antibiotics.

### **Challenges in Developing Animal Vaccines**

Infectious and fatal bacterial diseases are a major threat to all animals globally. Effective control of these bacterial diseases is of foremost importance to prevent economic losses due to mortalities among animals, safeguarding food security and combating rural poverty. Development of vaccines has led to healthier companion animals and disease-free poultry, livestock and fish in developed countries like USA and UK. However, challenges are still there that interfere with the development of veterinary vaccines that majorly include climate change that led to stability of pathogens and ultimately diseases in animals.

Zoonotic bacterial diseases like brucellosis are another concern to animal as well as human health so, preventing bacterial diseases in animals is critically important to protect world population from adverse disease outbreaks. Hence there is a need to develop new vaccines using advanced techniques to prevent infectious bacterial diseases in animals not only for animal health but also for welfare of humanity. Challenges in development of vaccines (Lewis & Roth, 2021) include antigenic variation, complex immune responses, adjuvant, delivery systems, economic considerations, short term immunity, vaccine stability, antibiotic resistance, host specificity of pathogens.

### **Mutations among Bacteria**

Bacteria have potential for mutations in their genes (Horton & Taylor, 2023) which lead to changes in their surface antigens, resulting in a new strain of bacteria under the same species. This phenomenon of mutation creates challenge in development of vaccines that have potential to target all strains of specific bacteria with efficacy. Some bacterial pathogens have the ability to stimulate both types of immune responses, i.e., Humoral and Cellular responses and form complex immune responses. Developing such kind of vaccine that can stimulate specific immune response type in required magnitude is a big challenge today.

Some bacteria are intracellular pathogens like *E. coli*, *Mycobacterium*, *Salmonella* etc. these bacteria replicate within the cells of host, developing a vaccine that work against these intracellular pathogens requires modern and costly equipment and strategies to specifically target these intracellular bacteria. Till now there are many types of adjuvants used (Zhao et al., 2023) in bacterial vaccines like Emulsion adjuvants, Aluminum adjuvants (Danielsson & Eriksson), Cytokines, Virosomes etc. that have the property of stimulating and enhancing the immune response, but the mechanism of action of adjuvants in enhancing the immune response is still unknown. Research is required in this area to know the actual mechanism of action of adjuvants, this will help in selecting the adjuvant which is both safe and effective in particular vaccine.

Another major issue in developing vaccines is cost and economic considerations as mutations in genetic material leads to new strains and antibiotic resistance, developing new vaccines each time mutations occurs is a costly and time-consuming process. In third world countries rural population is mainly involved in livestock and poultry production and cannot afford costly vaccines against bacterial diseases of economic importance like salmonellosis, colibacillosis, fowl cholera, mycoplasmosis, necrotic enteritis, black quarter, anthrax, enterotoxemia etc.

### **Public Awareness and Education on Animal Vaccination**

As there are various zoonotic diseases that transfer from animals to humans that are also fatal like rabies, public education and awareness regarding animal vaccination is crucial (Majumder et al., 2020) for ensuring health of both animals and humans. Vaccination helps to prevent the outbreak of contagious diseases with high mortality, promotes public health by monitoring zoonotic diseases and securing biodiversity worldwide.

There are misconceptions regarding animal vaccines majorly including vaccine safety, hesitancy, access to vaccines. Misconception regarding vaccine safety is that vaccines are harmful from health point of view and also it causes disease instead of preventing it. Public should be educated (Brand et al., 2023) that vaccines are extensively assessed for safety and efficacy before being used in veterinary side. From hesitancy point of view various pet owners, farmers, trainers hesitate using vaccines due to several reasons including cost, side effects like allergies, immunosuppression etc., and lack of awareness for preventing diseases. This issue can be addressed by educating people for benefits of vaccination against fatal contagious and zoonotic diseases.

At some areas in third world countries like India and Pakistan vaccination (Hussain et al., 2023) opportunities are not accessible and are extremely limited. Government together with veterinary organizations should work to ensure easy access to vaccines and vaccination programs. So, promoting vaccines and vaccination programs by educating public not only prevent zoonotic diseases and ensures public safety but also promises animal health and welfare.

### **Innovations in Vaccine Technology for Animal Health**

Vaccination uses on veterinary side has undergone necessary and adaptive changes from experimentation to risk free practice. Till now there are few bacterial diseases which have no vaccines and have adverse effect globally like contagious equine metritis, canine leptospirosis, bovine anaplasmosis, actinobacillosis etc. Investment in the Research and Development sector promises to overcome the gap (Ward & Wilson, 2020). Vaccination in animals is becoming popular now days due to advancement in research and innovative technologies to work in much better way and to achieve desired goals.

New techniques are made safe to use and effective in veterinary side. Recombinant viral vector vaccines, DNA vaccines, RNA vaccines these all vaccines fall under the category of third generation vaccines. Keeping in consideration the safety, potency, effectiveness, purity of vaccine, various animal diseases of bacterial origin have developed using recombinant DNA technology. These vaccines include rabies, canine distemper, avian influenza, Newcastle disease vaccines etc. Vaccines can even stay alive at room temperature and promises prevention from illness. On the other hand, vaccine delivery, design and administration are ultimate part of vaccine innovations with better immune activity.

In the field of adjuvants, nano adjuvants and new generation adjuvants are recent advancements in the innovation and advancement (Moni et al., 2023) of veterinary vaccines. Objectives of innovations in advances include enhanced immune stimulation, safety, improved drug delivery system, better immune response to antigens etc. The practices to make vaccines more effective also include designs based on existing drug delivery models and pharmaceutical principles under consideration to serve as immune stimulators or potentiators.

## Conclusion

Salmonellosis, Brucellosis, Leptospirosis etc. are some common bacterial infections in animals and have a significant impact on the animal's health and economy. Vaccination is an important preventive measure to avoid the prevalence of these diseases and to control the causalities from these pathogens. Immunization includes exposure to pathogens, host immune system activation, development of memory against that particular one antigen and its removal from body. Innate and adaptive immune systems play a role in providing immunization and both of these processes involve different cells & components. Live attenuated, killed, sub-unit, mRNA vaccine & DNA vaccines are the distinct types of vaccine in which different components of pathogen are used to initiate in immune response from the host. USDA, FDA, CVB & DRAP are the regulatory authorities that approve the use of vaccine after a long phase of testing. Vaccination process can lower the antibiotic resistance that is an emerging global issue. Development of different serotype, Immune system response, microenvironment of the cells, mutations in the bacterial cells & cost are some usual challenges for the development of curative vaccine. A lot of misconception about the use of vaccine can lead to fatal damage to the world, for this reason there must be a well understandable public awareness should be given. As this is the era of development, major changes have been emerged in the development of vaccination and these techniques will give benefit to the world.

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