Vaccines the tugboat for prevention-based animal production

20

Ramadevi Nimmanapalli and Vikas Gupta

Department of Veterinary Microbiology, Faculty of Veterinary and Animals Sciences, IAS, RGSC, Banaras Hindu University, Mirzapur, India

20.1 Introduction

Livestock farming is the most important sector of Indian agriculture and contributes in India's economy in terms of livelihood security. A total of 512.05 million livestock are present in India and most of these are reared by landless and marginal farmers and are the main source of their livelihood. Besides, organized sectors have also started showing interest in livestock farming; mainly in poultry and dairy sectors but their numbers are very small at the present. As livestock sector is a live market, they are very susceptible to different infectious diseases such as viral, bacterial, fungal, and parasitic diseases. These infectious diseases are posing a threat to the livestock production performance due to morbidity and mortality. Therefore keeping the livestock healthy to get better production is of paramount importance to agricultural economy. Vaccination of the animals against various infectious diseases prevailing in different geographical regions is the key measure of good husbandry practices and contributes a major role in maintaining animal health and minimizing economic losses due to production losses from infectious diseases.

The term vaccine ("vacca," meaning cow) was coined by Luis Pasteur in honor of Edward Jenner who used cowpox lesion as a substitute of smallpox scab to protect from smallpox infection in humans and establish the concept of vaccination. Around a century after him, Luis Pasteur made three vaccines for rabies, fowl cholera, and anthrax through the process of attenuation. Further, in 1886 Daniel Elmer Salmon and Theobald Smith gave the concept of inactivated or killed vaccine. Presently most of the vaccines used for immunization of animals or humans are either live or inactivated in nature. The conventional veterinary vaccines protect animals against the potential dangers of many infectious diseases. It stimulates the animal's immune system and prepares them to resist the infections caused by pathogenic microorganisms. Vaccination is the most effective way to prevent the transmission and the spread of animal disease epidemics which subsequently provide full security and public health.

The impact of veterinary vaccines is witnessed by the success of the Global Rinderpest Eradication Program which was a large-scale international collaboration involving vaccination, trade restrictions, and disease surveillance. This has been a great achievement in the animal health area and rinderpest is the second disease after smallpox eradicated globally. Vaccines against other diseases like brucellosis, rabies, foot and mouth disease (FMD) are being used as the main instruments in the eradication program of the respective diseases globally. In addition to assisting in the eradication program of animal diseases, vaccines also combat the emergence of drug-resistant pathogens and emergence of new diseases.

Since the first use of a vaccine, the research for vaccinology in the past 200 years has generated continuous technical breakthroughs and led to substantial improvements in human and animal health. Various developments have taken place with regard to types of vaccines and methods of immunization. However, it is only during the last two decades where the veterinary world has observed significant development of novel prophylactics which are facilitated by the advent of biotechnological tools and techniques, and discovery of antigen/gene delivery systems or recombinant vaccines developed using biotechnological tools or genetic engineering represents an alternative strategy by which the limitations of conventional vaccines are taken care of. A number of genetically-engineered vaccines which are rationally designed such as, live flavivirus chimera vaccine (WN-FV) (PreveNile), live double-gene deleted [deleted glycoprotein E (gE$^-$) and deleted thymidine kinase (tk$^-$)] bovine herpesirus type 1 strain (Hiprabovis IBR Marker), and feline immune deficiency vaccine (Fel-O-Vax) have already been introduced in the veterinary market.

The infectious animal diseases outbreaks are generally due to viruses, bacteria, or parasites. The vaccine against all pathogens is not available as there are some existing limitations in developed vaccines or difficulties in vaccine development. Reasons for unavailability of vaccines for certain diseases include that either it is not technically possible to develop vaccines that provide adequate protection against the etiological agent or it is not possible to develop safe and effective vaccines, or it may become ineffective in a short duration as pathogens change their characteristics. The vaccination cannot always be a universal option for control of animal epidemics. Many countries have vaccines against most viral or bacterial diseases but lack vaccines against parasitic diseases. Although there are difficulties in developing commercial vaccines against parasites, a few vaccines against parasitic infestation like coccidiosis in poultry and parasitic bronchitis in cattle caused by the nematode *Dictyocaulus viviparous* are available.

20.2 Vaccines and one health

For better public health food security, disease-free body and healthy ecosystems are the main tenets. These can only be achieved by coordinated approaches to

produce safe food, access to interdisciplinary medicine, and evaluation and reduced use of hazardous chemical and physical agents on the ecosystem. The World Health Organization (WHO), Food and Agriculture Organization, and the World Organization for Animal Health (OIE) together promoted a comprehensive approach for better public health called "one health" (McConnell, 2014). The objective of "one health" is to promote multisectoral response to food safety hazards, the risk from zoonotic diseases and its control (disease that can spread between animals and humans, e.g., rabies, West Nile fever, salmonella, and flu) (Vandersmissen and Welburn, 2014; Buttigieg, 2015). One health activity also includes public health threats at the human-animal-ecosystem interface (antibiotic resistance) and provides guidance on how to reduce these risks (Vandersmissen and Welburn, 2014; Hoelzer et al., 2018).

The world population is growing at a faster pace and is expected to reach more than 9 billion in 2050. Although, meat and egg production has increased between 1961 and 2007, there is a further need to increase production by 70% in order to fulfill the food security demand of projected world population of more than 9 billion people by 2050. Safe meats, eggs, and milk are essential to achieving the food security of a growing human population in the world and it is not possible without healthy livestock. Animals and poultry are susceptible to many infectious diseases and some cause food-born zoonoses in human beings. Veterinary vaccines contribute immensely to the maintenance of health and productivity of animals. The effective use of vaccines against various diseases could be an important component to meet present and future food demands.

In addition to preventing diseases against food animals, it is also important in preventing disease in companion animals and wildlife which subsequently has an important impact on reducing the incidence of zoonotic diseases in human. Vaccines for diseases of companion animals and horses have helped humans to keep animals in the household and enhanced human-animal bonding to enrich the lives of both animals and humans. Without rabies vaccines, it is unlikely that humans would have been willing to keep cats and dogs as pets.

Antibiotic resistance is the major concern in both veterinary and human medicine and arose due to excessive and indiscriminate application of antibiotics in treatment and as a feed additive in food animals. There are limited numbers of effective antibiotics for treatment against bacterial diseases but the possibilities of getting resistant against these are still a concern. Vaccine acts on the bacteria by eliciting host-immune response either through humoral or cell-mediated immunity and there is no possibility to get resistance against host immunity (Vandersmissen and Welburn, 2014; Hoelzer et al., 2018). Therefore vaccination is a safe and effective method to prevent bacterial infection in animals and humans. Bacterial vaccines minimize the treatment cost in food producing and companion animals which also involves the least use of antibiotics. Availability of inexpensive vaccines may reduce reliance on antibiotics for animal health.

20.3 Types of vaccines

20.3.1 Conventional vaccines

20.3.1.1 Live-attenuated vaccines

Live-attenuated vaccine is a live microorganism with very little or no pathogenicity which cannot cause disease but has the ability to induce protective immunity. Generally, they are produced by serial passages of agents in unnatural or heterologous hosts or cell lines and sometimes distant relative of pathogenic microorganisms which are not pathogenic to the target host (Jorge and Dellagostin, 2017). Viruses acquire random mutations in their genome after multiple serial passages in heterologous systems leading to loss of pathogenicity without compromise in immunogenicity (Meeusen et al., 2007). They are able to replicate in the host and induce both cellular and humoral immunity. The immunity generated by live vaccines persist a longer duration and there is no need for adjuvant (van Gelder and Makoschey, 2012; Jorge and Dellagostin, 2017). The limitations of live vaccines are adverse reaction and reversion of virulence inside the host. Besides, they have less shelf-life and are sensitive to high temperature. Therefore they require cold chain or refrigeration for storage and transportation. Examples: *Brucella abortus* S-19, *Peste-des-petits ruminants* virus vaccine, sheeppox vaccine, canine parvovirus vaccine, canine distemper vaccine, Newcastle vaccine, etc.

20.3.1.2 Inactivated vaccines

Inactivated vaccines consist of killed bacteria or virus of one or more species or serotypes, mixed with an appropriate adjuvant (Jorge and Dellagostin, 2017). The vaccine microorganism is usually grown in bulk in a suitable system (cell culture, egg embryo, or bacterial media) and inactivated by physical (heat and ultraviolet-rays) or chemical means (formaldehyde, beta-propiolactone, and binary ethyleneimine) which denature either surface proteins (surface effect) or damage the nucleic acid of vaccine virus (Meeusen et al., 2007). The inactivated microorganism may be further purified and mixed with a suitable adjuvant (van Gelder and Makoschey, 2012). These vaccines are comparatively easy to produce than live vaccines but provide a shorter duration of immunity. Further, most of the viruses have multiple serotypes or continuously changing antigenic structures (e.g., FMD virus and influenza viruses) and one serotype does not provide protection to other serotypes, therefore, vaccine candidates for inactivated vaccines should be continuously evaluated to provide coverage against the outbreaks. Examples of such include FMD vaccine, bluetongue virus vaccine, bovine viral diarrhea virus vaccine, rabies virus vaccines, etc.

20.3.1.3 Toxoids

The diseases caused by bacterial toxins are also controlled by vaccination. The vaccines against diseases of toxins' origin are produced by inactivating native toxins by physical or chemical means and mixed with adjuvants (Jorge and

Dellagostin, 2017). However, they also possess some limitation of biological safety. The use of recombinant DNA technology can overcome these limitations, and can produce toxoid in bulk with safety. For example, the production of recombinant toxins does not require many biosafety precautions because the toxic domain of the protein is removed by biotechnological tool (Arimitsu et al., 2004). Examples of such include tetanus toxoid, anthrax protective antigen toxoid, and clostridium type A toxoid, etc.

20.3.2 Genetically-engineered vaccine

20.3.2.1 Subunit vaccine

Subunit vaccines contain one or more fragments or full-length proteins of a pathogen instead of the whole pathogen to elicit protective immunity in the host (Jorge and Dellagostin, 2017). Compared to conventional vaccines, these vaccines are safe to administer, nonreplicating, easy to produce, cost effective, and have no deleterious effect due to unwanted antigenic materials. They can be made by isolating antigenic protein(s) from any infectious organism after its disruption. This type of strategy is common in aviral subunit vaccine called split vaccine. The recombinant subunit vaccines are made by identification and selection of protective antigen gene coding region followed by their cloning in suitable vector and expression in a heterologous host system such as bacteria, yeast, mammalian and insect. *Escherichia coli* is used extensively for protein expression as heterologous host besides limitation in the form of yield, posttranslational modification and folding of expressed recombinant proteins. The limitations of *E. coli* expression system were improved by the introduction of methylotropic yeast (*Pichia pastoris*) which has the capacity of posttranslational modification and folding of expressed recombinant proteins. Since the subunit vaccines induce less immunity in comparison to whole bacteria or viral vaccine, they are used with a suitable adjuvant. Examples of such include Newcastle disease virus (NDV) subunit vaccine using hemagglutinin-neuraminidase (HN) gene, FMDV subunit vaccine using VP-1 gene, porcine circovirus type-2 (PCV-2) subunit vaccine based on open reading frame-2 (commercialized) and prM, and E envelope protein-based subunit vaccine of Japanese encephalitis.

20.3.2.2 Virus-like particle vaccines

Multiprotein structures that mimic the conformation and authentic structure of an empty viral capsid but are devoid of genetic material are called virus-like particles (VLPs). They are nonreplicating and but contain an array of antigens similar to the outer structure of virion (Jennings and Bachmann, 2008). Since their structure and antigenic surface resemble virion, they are able to elicit both humoral and cell-mediated immune responses without the need of adjuvant (Jorge and Dellagostin, 2017). Further, they are safe due to the absence of genome and provide a high degree of protection without the possibility of reversion of virulence.

They could provide a promising differentiation of infected from vaccinated animals (DIVA) strategy during serosurveillance and eradication program of disease. Therefore they may be a better substitute for inactivated and live vaccines. VLP has been successfully employed in two licensed vaccines, hepatitis B and human papilloma virus but there is no report of licensed veterinary vaccine until now.

20.3.2.3 Vectored vaccines

The live vector, having the foreign protective antigen coding gene of a bacteria or virus used for eliciting the immune response against the protective antigen is called a vectored vaccine. The live vectors are attenuated virus or bacteria which act as a backbone to deliver large amounts of exogenous gene inside the host (Jorge and Dellagostin, 2017). A number of viruses (vaccinia virus, canary pox, fowlpox, and adenovirus) and bacteria [Bacille Calmette-Guérin (BCG), *Listeria monocytogenes*, *Salmonella* spp., and *Shigellae* spp.] have been tested for their capability to carry the heterologous genes and their expression inside the host (Rizzi et al., 2012). They provide long lasting immunity due to being viable in nature and because they do not need any adjuvant. Currently, the canary poxvirus vector system has been used for vaccines against rabies virus, canine distemper virus, feline leukemia virus, and equine influenza virus. The bacterial recombinant BCG has significant potential to express a large number of antigens and can induce solid immunity. The use of transgenic plants engineered to produce and deliver immunogenic antigens via food sources has potential perspective in vaccine industries. In veterinary vaccinology, transgenic plants are able to produce and deliver antigens through animal feed. Plant-based vaccine trials have been conducted for various parasitic diseases including poultry coccidiosis, schistosomosis, porcine cysticercosis, and ascariosis. Plant-derived rabies G protein expressed in tomato, tobacco, and spinach on oral administration in mice mount local and systemic immune response (Shams, 2005). Besides, in attempt to form edible vaccine for rabies, vaccinia, canarypox, adenovirus, and yeast; they were employed for expression of neutralizing G protein of rabies and used as a delivery system. Rabies vaccine in the form of consumable bait (edible vaccine; raboral V-RG coated in fishmeal and fish oil) was successfully used for vaccination of wildlife such as raccoon, fox, etc.

20.3.2.4 DNA vaccine

Naked DNA plasmid having the protein coding gene of viral, bacteria, or parasites and that can express it in mammalian cells are defined as DNA vaccine (Paludan and Bowie, 2013). In addition to a desired exogenous antigenic gene, the plasmid contains a strong eukaryotic promoter, polyA tail, multiple cloning sites, and suitable selective marker. The basic aim of DNA vaccine system is that the antigen can be expressed directly by the cells of the host in a way similar to that occurring during viral infection and expressed antigen after processing will be represented either via major histocompatibility complex-I or major histocompatibility complex-II leading to cellular and humoral immune responses

(Shi et al., 2014; Meeusen et al., 2007). They are easy to manufacture, have low cost, and do not require cold chain facility. DNA vaccines were administrated either by intramuscular (*I/M*) injection or using a DNA particle delivery system called gene gun. Immunization of animals with DNA vaccine is comparatively safer than the use of other conventional vaccines as later unnecessarily expose the host to a wide variety of antigen (Jorge and Dellagostin, 2017). However, there is concern regarding possible integration of DNA in the host genome and might be inactivation of a tumor suppressor gene. A few examples of DNA vaccines are West Nile virus vaccine (first approved DNA vaccine), influenza virus DNA vaccine (passed clinical trial for ponies), and feline immune deficiency virus.

20.4 Developments in veterinary vaccinology

Since, the discovery of the smallpox vaccine by Jenner in the 19th century, various forms of vaccines have been developed by using advanced recombination technology (Jorge and Dellagostin, 2017). Around two to three decades ago the veterinary vaccines used were mostly live attenuated, inactivated vaccines and toxoid but with recent advances in immunology and molecular biology, and sophisticated forms of genetically-engineered vaccines have been introduced. Although, live-attenuated vaccines are able to induce both cellular and humoral immune responses, they also can produce some side effects. Killed/inactivated vaccines are typically safer but may be less effective than attenuated vaccines whereas, commercial vaccines based on toxoids are difficult to produce. The side reactions, safety issues, effectiveness, etc. are certain issues of aforementioned vaccine and warranted the requirement of better and safer vaccines which can help in the prevention and control of animal diseases.

A genetically-engineered vaccine has the potential to alleviate limitations of conventional vaccines. Efforts to develop more effective vaccines against a large number of diseases using genetic engineering are in progress around the world. Genetically-engineered or recombinant vaccines are developed based on rationally designed recombinant and highly purified antigens through epitopes mapping and their prediction. Currently, a number of subunit or vectored veterinary vaccines using biotechnological tool have been commercialized (Table 20.1).

20.5 Diversity of vaccine

20.5.1 Bacterial diseases

20.5.1.1 Hemorrhagic septicemia

Hemorrhagic septicemia (HS), an acute and highly fatal disease of cattle and buffalo, is caused by *Pasteurella multocida*. HS occurs as catastrophic epizootics in

Table 20.1 A list of recombinant veterinary vaccine.

Animal species	Pathogens	Vaccine type
Cats	Feline leukemia virus	Canarypox virus Vector
Cats	Rabies virus	Newcastle disease virus (NDV) and canarypox vector
Cattle	*Ripcephalus (Boophilus) microplus*	*Babesia bovis*
Dog	Canine distemper virus	Canarypox vector
Ferrets	Canine distemper virus	Canarypox vector
Horse	Influenza virus and tetanus toxin	Canarypox vector
Horse	Influenza virus	Canarypox vector
Horse	West Nile virus	Canarypox/ALVAC vector
Horse	West Nile virus	DNA vaccine
Poultry	Infectious laryngotracheitis	Fowlpox vector
Poultry	Avian influenza	Fowlpox virus, NDV, herpes virus of turkey, duck enteritis herpes vector
Poultry	Marek's disease	Herpes virus of turkey vector
Poultry	Newcastle disease	Modified NDV
Poultry	*Mycoplasma gallisepticum*	Fowlpox vector
Racoon/coyotes	Rabies virus	Racoon poxvirus vector
Sheep/goat	*Echinococcus granulosus*	Subunit
Swine	Classical swine fever virus	Recombinant adenovirus vector
Swine	Porcine circovirus	Subunit
Swine	*Actinobacillus pleuropneumoniae*	Subunit
Swine	Porcine circovirus	Swinepox vector
Swine	Porcine circovirus	Subunit

From Jorge, S., Dellagostin, O.A., 2017. The development of veterinary vaccines: a review of traditional methods and modern biotechnology approaches. Biotechnol. Res. Innov. 1, 6–13.

many Asian and African countries, resulting in high mortality and morbidity (De Alwis, 1992; Verma and Jaiswal, 1998). Although, antibiotics is the main therapeutic to treat the disease and control the incidence of such microbial infection, remains of antibiotics in animal products and antibiotic resistance are the drawback of antibiotics use. The other alternative to control and prevention of HS is by vaccination of animals in endemic areas prior to the expected outbreak of HS.

Immunity generated in HS is serotype-specific therefore selection of vaccine candidates depend upon circulating serotypes in that geographical regions. Various strategies have been used to develop HS vaccines such as killed vaccines (bacterins), live-attenuated, cellular vaccines, and genetically-engineered vaccines (Myint et al., 1987; Verma and Jaiswal, 1998; Hodgson et al., 2005). But killed vaccines are used commonly for the vaccination against HS. Bacterins used against HS include formalized bacterin, aluminum hydroxide gel, and oil adjuvant vaccines (OIE, 2017). Among these, aluminum hydroxide gel vaccine and oil adjuvant vaccines elicit a good immune response in the studies conducted in many Asian countries including India during the last few years, and are the vaccine of choice.

20.5.1.2 Brucellosis

Brucellosis is one of the most important bacterial zoonoses worldwide and characterized with significant economic losses in terms of reproductive performance of dairy animals and posing a continuous threat for human community (OIE, 2017). Disease has wide host range and it is primarily caused by *Brucella abortus* and *Brucella melitensis* in large (cattle) and small ruminant (goat) respectively (OIE, 2017). Abortions in late gestation, placentitis, epididymitis, and orchitis are the most common consequences. Direct or indirect contact and consumption of products from infected animals act as a source of human brucellosis. Therefore WHO, OIE, and other agencies collectively set a plan under one health program to control the brucellosis. Animal brucellosis can be prevented by applying good managemental and hygienic practices. Countries having a low prevalence of brucellosis are following the test and slaughter policy while it is not economical in highly endemic counties and vaccination is the only option. Currently, live-attenuated *B. abortus* strain 19 and RB-51 are used for immunization of cattle while *B. melitensis* Rev 1 is used for sheep and goat (Moriyón et al., 2004; Corbel, 2006). Most of the countries are using *B. abortus* strain 19 to immunize cattle because of its high protective efficacy, although it induces abortion in pregnant animals and is not capable of DIVA. While RB-51 is not abortogenic and capable of DIVA strategy due to lack of O-antigen of LPS and has similar protective efficacy. New generation vaccine strains based on attenuation organism, protein subunit, and DNA fragments were also tested experimentally to get safer vaccines (Golshani and Buozari, 2017) but none of them are yet commercialized for immunization purpose. Further, killed *B. abortus* 45/20 and *B. melitensis* H38 are also available but are less protective (Schurig et al., 2002; Plommet et al., 1970).

20.5.1.3 Anthrax

Anthrax organism is a dreaded pathogen of animals and humans characterized by septicemia, sudden death, and oozing of blood from natural orifices of animals. It is caused by a gram-positive, nonmotile and spore-forming bacteria *Bacillus anthracis* (Kaur et al., 2013). The morbidity and mortality are very high and the affected animals or their remains are a constant threat to humans and other susceptible animals. The animals can be protected by vaccination with a single dose

of sterne spore vaccine which is an attenuated noncapsulated spore-forming anthrax bacilli (Grabenstein, 2003). Besides, the protective antigen of *B. anthracis* is also used to immunize the animals in toxoids form (Kaur et al., 2013). Further, *E. coli* expressed protective antigen of anthrax bacillus (cap$^+$ Tox$^+$) was also evaluated in New Zealand white and rhesus macaques but until today there was no commercialized recombinant vaccine for field use (Chawla et al., 2009; Kaur et al., 2013).

20.5.1.4 Black quarter

Black quarter is a fatal infectious disease of cattle, and some other ruminants characterized by fever, myonecrosis of active muscles, edema, lameness, and death. The disease is caused by gram-positive, endospore-forming, histotrophic anaerobic bacteria *Clostridium chauvoei* (Abreu et al., 2017). It generally affects unvaccinated healthy cattle of 6−24 months of age causing high mortality and significant economic loss. Blackleg is a preventable disease and formalin-treated culture of *C. chauvoei* formulated with alum as an adjuvant and chemically toxoid culture supernatant are used worldwide for immunization of susceptible groups (Uzal, 2012). Additionally, purified flagellin, crude cell wall proteins, and recombinant CctA were also shown to be promising antigens to induce protective immunity (Frey and Falquet, 2015).

20.5.1.5 Leptospirosis

Leptospirosis is a neglected zoonotic disease of humans and animals, caused by *Leptospira* spp. (Bharti et al., 2003). The disease is characterized by fever, icterus, vomiting, dysentery, dehydration, petechiae of pleura, hemoglobinuria, and grayish white focal necrotic lesions of kidneys. Leptospirosis is a major public health important disease in developing, improvised countries and causes huge production loss in animal husbandry. Current vaccines used for immunization are based on whole cell killed preparation (bacterin), cell membrane extract, and purified outer envelope (Bolin et al., 1991; Cullen et al., 2002; Bharti et al., 2003). Most killed vaccines are of animal use while very few are licensed for human use. The immunity of *Leptospira* is serovar-specific and there are so many types of serovars present worldwide therefore multivalent bacterin formulations having locally prevalent serovar are used for immunization of cattle, pigs, and dogs worldwide (Bolin et al., 1991). Some recombinant vaccines based on outer membrane proteins, leptospira immunoglobuline-like proteins, and lipoproteins of leptospira were also experimentally evaluated but none of them are available for immunization purpose (Silveira et al., 2017; Faine et al., 1999; Levett, 2001).

20.5.1.6 Mycobacterium infection in cattle

Tuberculosis and paratuberculosis are chronic diseases of ruminants caused by *Mycobacterium bovis* and *M. avium* subsp. *paratuberculosis* respectively (Palmer et al., 2011). Bovine paratuberculosis is an infectious, granulomatous disease leading to loss of animal health while paratuberculosis (Johne's disease) is

clinically characterized with chronic shooting diarrhea and emaciation (Gilardoni et al., 2012). Both diseases are collectively causing huge economic loss of the dairy industry worldwide. *M. bovis* also causes infection in human beings and is one of the major zoonosis concerns of the present time (Grang, 2001). Besides, *M. tuberculosis*, a pathogen of humans may also infect domestic animals and these infected animals become the source of its further transmission to other susceptible animals and human beings. This phenomenon is called reverse zoonosis. Mycobacterial infection shows synergism with human immunodeficiency virus (HIV) infection in human beings and HIV/*M. tuberculosis* (dangerous couple model) copandemic is occurring and claiming million of lives each year (Shankar et al., 2014). Crohn's disease, a chronic inflammatory intestinal condition of human beings is considered to be caused by *M. avium* subsp. *paratuberculosis*. Good management practices and test and slaughter policy are used for the control and prevention of these diseases in bovines. The efficacy of a live vaccine made from the attenuated strain of *M. bovis*, BCG has proven variable and use of this vaccine might hinder the interpretation of current diagnostic tests (Balseiro et al., 2017; Cousins, 2001).

20.5.1.7 Salmonellosis

Salmonella organisms are an infectious pathogen that infects animals and humans both (Kemal, 2014). In bovine, the disease is characterized by septicemia, acute or chronic enteritis and abortions (Kemal, 2014). Bovine salmonellosis is caused by *Salmonella* Dublin and *Salmonella typhimurium*. Salmonellosis has a significant economic impact on dairy and beef farming due to poor quality of milk and meat (McEvoy et al., 2003). Besides, it also possesses human health concerns due to the consumption of contaminated meat and milk, and close contact of the animal's handlers and veterinarians. Further, *Salmonella* isolates particularly *S. typhimurium* definitive type 104 and have develops resistance to multiple antibiotics and can act as donor for resistant determinant to other opportunistic bacteria found as commensal in intestine (Piddock, 2002). Therefore to avoid possibility of evolution of new resistant bacteria and disease manifestation in animals and humans, vaccination is the most important tool along with good animal husbandry practices. Both inactivated and modified live (MLV) *Salmonella* vaccines are licensed for immunization of cattle (Danielle, 2006; Adem and Bushra, 2016). Most of the inactivated commercial vaccines are bivalent in nature and have *S.* Dublin and *S. typhimurium* formulated with suitable adjuvant (aluminum hydroxide). A genetically- altered aroA mutant *S.* Dublin live vaccine is also used for immunization of farm animals in different developed countries (Duncan et al., 1987). Further, gram-negative core antigen bacterins such as ENDOVAC-Bovi (*S. typhimurium* lacking polysaccharide repeat of LPS) and J5 or J5-VAC (LPS core antigen made from mutant strain of *E. coli*) are commercially available, and it is claiming that they can cross protect animals from other endotoxin-producing bacteria such as *E. coli*, *Salmonella*, *P. multocida*, and *Manheimia hemolytica*. Besides, autogenous vaccines are also recommended to protect animals on the basis of prevalent *Salmonella* types on farms.

20.5.1.8 Escherichia coli *infection*

E. coli is a gram-negative bacilli found as normal intestinal flora of animals and humans, and very few are pathogenic in nature which can cause illness in animals and humans. Generally, healthy animals act as a reservoir of *E. coli* and asymptomatically shed the *E. coli* in the environment. Pathogenic *E. coli* of animals (cattle, sheep, pig, and goat, etc.) are diarrheagenic *E. coli* (DEC), uropathogenic *E. coli*, septicemic *E. coli*, [includes avian-pathogenic *E. coli*], and the mammary-pathogenic *E. coli*. Enterotoxigenic *E. coli* (ETEC) producing enterotoxins in pigs and ruminants leads to hyper-secretary diarrhea and electrolytes loss, and the enteropathogenic *E. coli* causes attaching and effacing (A/E) lesions in most mammals come under the DEC (Hebbelstrup Jensen et al., 2014). *E. coli* producing Shiga toxin STx2e (Shiga toxin-producing *E. coli*, STEC, verotoxigenic *E. coli* or VTEC), is the cause of edema disease in pigs, whereas cattle that produce STx and A/E lesions cause subclinical or nonclinical infections in ruminants (Smith, 2014). Enterohaemorrhagic *E. coli* (EHEC) causes severe illness in children and the elderly. Clinical sings depend upon types of infections in animals. Clinical manifestations caused by *E. coli* infection are enteric colibacilosis, colisepticaemia, edema disease, and coliform mastitis, etc. in young (calves, lambs, chicks, and piglets) and adult animals, leading to economic losses (Stein and Katz, 2017). Besides, infected animals are also a potential source for human infections. ETEC infection is a noninvasive type of gastrointestinal infection, and mucosal immunity plays an important role in colonization of these bacteria. Therefore killed bacteria with fimbria or extracted fimbria with or without LT toxoid (heat labile enterotoxin) are used for immunization of dams before parturition. Commercial vaccines for cows include *E. coli* F5 isolates or F5 adhesin while purified F4, F5, F6, or F41 fimbria or killed *E. coli* expressing these fimbriae with or without LT toxoid are used for immunization of sows. Further, live-attenuated, oral subunit vaccine having purified fimbria and poly (lactide co glycolide) (PLGA)-encapsulated fimbria or live vaccine was also evaluated for prevention of colonization (Edelman et al., 1993). For prevention of EHEC, whole bacteria, adhesin-intimin, fimbria, type III secretion system were tried (Smith, 2014) and the most successful vaccine is live recombinant *Salmonella* Dublin expressing *E. coli* O157:H7 intimin (Khare et al., 2010). Recently, SPR vaccine (bacterial extract siderophore receptor and porin, SRP technology) targeting *E. coli* O157 serotype is licensed for use in cattle to reduce the amount of *E. coli* O157 pathogen (Fox et al., 2009).

20.5.2 Viral diseases

20.5.2.1 Foot and mouth disease

A very infectious and contagious disease of cloven-hoofed mammals caused by FMDV has seven serotypes (O, A. Asia-1, C and SAT-1, 2, 3) and each serotype has different variants (Jamal and Belsham, 2013; Poonsuk et al., 2018). The

disease is characterized by high fever, lameness, formation of blister on mucosa of mouth, tongue, teats, and hoof. The disease has high morbidity and low mortality and affects all age groups of cattle. Due to high morbidity, the disease causes massive production loss and is considered as an economically important disease and a threat to livestock production worldwide. For the control of disease, virus (harvested from BHK-21 cell line) inactivated with binary-ethyleneimine is formulated with saponin/aluminum hydroxide or various oil-based adjuvant is used to potentiate the protective immune response in susceptible animals (Grubman and Baxt, 2004). Immunity induces by one serotype or subtype does not protect animals from other serotypes or subtypes of FMDV infection. Therefore which serotype or subtype is used as a vaccine candidate depends on the circulating FMDV type in that geographical areas/ countries. In India, trivalent vaccine having "O, Asia-1 and A" serotypes are being used for vaccination of cattle and buffaloes (Jamal and Belsham, 2013). Different FMDV eradication programs were launched in various countries, and disease was successfully eliminated from Western Europe and part of South America. But, the disease is still circulating in most parts of the world and posing a constant threat to dairy husbandry. Further, low quality vaccines, the simultaneous presence of various circulating types of FMDV in different countries and wildlife reservoir (African buffalo) are the main constraints in the control and eradication of this dreaded disease.

20.5.2.2 Rabies

Rabies is a neglected zoonotic fatal disease of warm-blooded animals including human beings, and caused by rabies virus. It is associated with exposure of rabid animals, and incubation period of the disease depends on the extent of bite, site of bite from the brain, and quantum of virus entered by saliva at the bite wound (Blanton et al., 2009). The disease is reported from all the geographical areas of the world except Antarctica and has around 100% mortality in humans and animals. Over the last 100 years, a number of vaccines such as inactivated, MLV, and recombinant have been developed for the control and prevention of disease (Muller et al., 2001; Xiang et al., 2003; Singh et al., 2017). The neural origin vaccines have been discontinued due to their adverse effects and use of animals for the propagation of the virus. Nowadays modern vaccines, cell culture, and embryonated egg-based inactivated vaccines (Beta-propiolactone) are being used prophylactically (preexposure) and therapeutically (postexposure) to protect humans and animals against rabies (Singh et al., 2017). These modern vaccines are now available in most developing countries and have been successful to minimize the number of human exposures. Further, recombinant vaccines lack residual pathogenicity caused by rabies because they contain only single nonvirulent gene products. Various vectors such as animal poxvirus, human and canine adenoviruses encoding rabies virus glycoprotein G have been tested in different targets (dog, cat, fox, and raccoon) and nontarget wild animals via oral route (rabbit, deer, etc.). Among these vaccines, a vaccinia-based recombinant vaccine is used for immunization of wild animals as edible bait and are playing an important role in

the prevention of rabies virus from wild animals to other domestic animals and humans (Yang et al., 2013). The oral vaccines are Raboral V-RG (vaccinia recombinant virus expressing G protein) and with Rabigen SAG2 (double mutant avirulent strain SAG2).

20.5.2.3 Peste-des-petits ruminants

It is an acute, highly contagious viral disease of small ruminants characterized by fever, loss of appetite, stomatitis, gastroenteritis, and pneumonia (Muthuchelvan et al., 2015). The disease is markedly evident in goats. Goats are more susceptible to PPR compared to sheep. Transmission occurs by direct contact of infected goats and sheep, through contaminated food, water, beddings, and feces. The disease may spread in a flock through the introduction of newly purchased sick animals from the market. The disease has a serious economic impact in terms of high morbidity and mortality as well as reduces production ability. Vaccination is the most effective way to control PPR. An earlier practice to control the disease was to immunize the animals with Plowright's live-attenuated tissue culture rinderpest vaccine (heterologous vaccine) but its use was stopped due to hindrance in the serosurveillance of rinderpest (Muthuchelvan et al., 2015). Further, homologous PPR virus was used after passage in vero cell line. Presently, Nigeria75/1 strain of Africa, Sungri-96 strain isolated from goats developed by IVRI, Mukteswar or Arasur-87 strain of peste-des-petits ruminants (PPRV) isolated from sheep by TANUVAS are used for immunization of goat and sheep (Diallo et al., 1989, 2007; Palaniswami et al., 2005; Singh et al., 2004). These vaccines are efficacious, safe, and provide a long-term protection to small ruminants.

20.5.2.4 Bluetongue

It is an acute but noncontagious disease of sheep characterized by fever, inflammation, and ulceration of buccal mucosa and tongue (Chand et al., 2015; Mayo et al., 2017). It is caused by the bluetongue virus (BTV) which has at least 27 different serotypes worldwide. The disease is transmitted by *Culicoides* species and affects mostly sheep, goats, and rarely cattle (Chand et al., 2015; Mayo et al., 2017). The disease is prevalent in rainy seasons. For the control of disease besides management practice as well as vector control, immunization of susceptible animals is a more effective strategy. Presently, MLV vaccine and inactivated vaccines are used for the control of the disease in various continents of the world (Bhanuprakash et al., 2009; Chand et al., 2015). As the immunity in BTV is serotype-specific and there are so many circulating serotypes in a geographical area at a time, the vaccine formulation is very difficult and challenging. Because of this reason, multivalent vaccines are used for immunization of animals. MLV vaccine produces viremia in animals which leads to further transmission of the virus and causes abortion, therefore this vaccine is generally not recommended for vaccination. Most of the countries are using inactivated BTV virus using BEI and hydroxylamine (Ramakrishnan et al., 2006). Presently in India pentavalent vaccine having BTV-1, 2, 10, 16, and 23 serotypes are used for the vaccination

(Reddy et al., 2010). VLP-based genetically-engineered vaccine was also attempted but due to serotype-specific immunity and genetic drift in serotypes, this strategy was not successful (Chand et al., 2015).

20.5.2.5 Sheep pox and goat pox

Sheep pox and goat pox are diseases of sheep and goats caused by sheep pox (SPV) and goat pox virus (GPV) of the genus *Capripoxvirus* and characterized with pyrexia, generalized lesion, internal pox lesion, and lymphadenopathy (Bhanuprakash et al., 2011; Madhavan et al., 2016). In a susceptible herd, morbidity and mortality are 75%−100% and 10%−85% respectively depending upon virulence of infecting virus strains. Most strains are host-specific and cause severe clinical manifestations in sheep or goat while some strains are equally virulent in both sheep and goats. For the prevention of disease both live-attenuated and inactivated vaccines are available, however inactivated vaccine provides a short duration of protection (Bhanuprakash et al., 2012; Boumart et al., 2016). Live-attenuated vaccine elicits long-term protection against SPV and GPV but its use is limited due to stimulation of pock lesion or death for some animals. Usually, the homologous vaccination strategy is useful for the protection of animals and locally prevalent strains are used as vaccine strains for immunization of sheep and goats (Rao and Bandyopadhyay, 2000). In India, live-attenuated vaccine incorporated with RM-65 strain for sheep pox and Uttarkashi strain of goat pox is currently used for immunization of sheep and goats, respectively (Madhavan et al., 2016).

20.5.2.6 Classical swine fever

It is an acute, highly infectious viral disease of swine of all ages characterized by rapid and sudden onset, high morbidity, mortality, and generalized hemorrhages (Blome et al., 2017). It has a massive impact on pig industries and is therefore notifiable to the OIE (2017). For prevention of disease live-attenuated vaccines are used. Currently, live-attenuated vaccine strains such as Chinese strain, Weybridge strain, Thiverval and lapinized virus, produced by the repeated passage of virus in tissue culture of porcine origin (PK-15) and rabbit are used for immunization of pigs (Blome et al., 2017). Additionally, E2 protein- based marker vaccine is also used for differentiation between infected and vaccinated animals (Huang et al., 2014). Recently a chimeric pestivirus vaccine "CP7_E2alf" was found safe and efficacious following oral administration and licensed for the oral immunization of pig (Eblé et al., 2014a,b).

20.5.2.7 Japanese encephalitis virus

Japanese encephalitis (JV) is a zoonotic viral encephalitic disease with high morbidity and mortality in human and livestock. The causative agent of this vector-born disease is Japanese encephalitis virus (JEV), a member of genus *Flavivirus* and transmitted by thebite of *Culex* mosquitoes (Basu and Dutta, 2017). Generally, JEV maintained in a natural cycle between mosquitoes and water bird,

and pig acts as an amplifying host (Yun and Lee, 2014). Accidentally, at peak of mosquitoes' prevalence in rainy seasons, the virus also infects dead-end hosts; human and horse due to mosquitoes' bite. Infections in pigs lead to significant reproductive problems causing abortion, still-birth, and birth defects while horses suffer from pyrexia and neurological manifestations leading to death (Lindahl et al., 2013). Both inactivated and live-attenuated vaccines are available for pigs, horses, and humans. MLV [produced in hamster or swine kidney tissue culture or hamster lung (HmLu) cell line] and inactivated (prepared in mouse brain, chicken embryo eggs, or cell lines, e.g., vero cells) are used for immunization of pigs and horses (Basu and Dutta, 2017). A genetically-engineered JE vaccine that combines the attenuated JEV strain and yellow fever vaccine virus is also available for humans (Janewongwirot et al., 2016).

20.5.2.8 Bovine viral diarrhea
It is an economically important infectious disease that affects a wide range of animals belonging to order *Artyodactyla*, including cattle, sheep, goat, camel, pig, and other domestic and wild ruminants, manifested with reproductive, respiratory, and gastrointestinal alignments. The disease is enlisted in the OIE. The disease is caused by bovine viral diarrhea virus-1 (BVDV-1) and bovine viral diarrhea virus-2 (BVDV-2) belong to genus *Pestivirus* of *Flaviviridae* family. At present at least 21 (BVDV-1a−1u) and 4 (BVDV2a−2d) subgenotypes of BVDV-1 and BVDV-2, respectively have been identified. On the basis of cytopathic effect on cell culture, each genotype is further classified into cytopathic (CP) and noncytopathic (NCP) biotypes. The clinical infections are of, acute and transient infection in immune-compromised cattle and persistent infection in new born calf when the virus infects the dam in the first trimester of gestation (before the development of the immune system) and chronic infection due to the invasion of virus in immune-privileged sites. The persistently infected (PI) animals act as a major source of disease transmission in the herd due to constant shedding of virus from all secretions. Economic impact in terms of reduction in milk yield, loss of fetus due abortion, still-birth, mummification, and low body score, led various countries to start a control program to curtail and eradicate the disease from the livestock population. In order to control and prevent, prophylactic vaccination of susceptible animals and test and culling strategy depending upon seroprevalence of disease, cattle density, and trade has been adopted in European countries and results were quite convincing. The primary goal of prophylactic vaccination against BVDV is to protect the fetus from in-utero infection to avoid birth of new PI calves. Both MLV and inactivated vaccines are used for immunization of animals (Beer et al., 2000). It is considered that inactivated vaccine is safer than MLV and therefore MLV vaccine is not recommended to pregnant animals in their first 6 months. In contrast to NCP biotypes, most modern modified-live vaccines use CP biotypes of BVDV as these types of virus are not able to establish persistent infection in fetus. A *Npro* gene deleted and endoribonuclease activity inactivated NCP BVDV mutant was developed to deal with safety concerns which

is not able to cross the placenta and provides immunity similar to field type BVDV. Marker vaccines based on glycoprotein E-2 expressed in baculovirus or transgenic plant and BVDV E-2 DNA vaccines have also been evaluated for immune response (Thomas et al., 2013). Recently, truncated glycoprotein E-2 fused with single chain antibody (APCH) subunit vaccine (Pecora et al., 2015) (Vedevax) expressed in baculovirus was commercialized for field use. Protective immune response in BVDV is genotype-specific and is not effective in conferring cross- protection to heterologous genotypes. Therefore vaccine formulations require either one or both genotypes depending upon the prevalence of BVDV in a particular continent or geographical strata. To address this aforementioned problem, a novel mosaic polypeptide chimeras having three protective determinants; of BVDV-1a, BVDV-1b and BVDV-2 genotypes using adenovirus vector construct (adBVDV prototype vaccine) was evaluated and found better immunogenic with heterologous protection (Lokhandwala et al., 2017).

20.5.2.9 Infectious bovine rhinotracheitis

It is one of the agents of bovine respiratory disease complex characterized by inflammation of nose and trachea of cattle. Bovine herpesvirus-1 (BoHV-1), a member of *alphaherpesevirus* is the etiological agent of IBR. This virus also causes infectious pustular vulvovaginitis in cows and infectious pustular balanoposthitis in bulls. Latency inside sensory ganglion is the most unique feature of BoHV-1 which is also seen in other herpes viral infections. Latent animals become clinically infected once again due to recrudescence of virus by stressful stimuli and subsequent reexcretion of infectious virus acts as a source of infection for other susceptible animals of the herd. It is a major economic problem in dairy and beef industries of the world due to huge production losses in the form of reduced milk yield, abortion, and less weight gain. The biosecurity, test and culling, and prophylactic immunization are used for control of the disease. Around 200 vaccines have been licensed for immunization against IBR worldwide. Among these most are conventional types (nonmarker) while very few are marker types. Conventional vaccines include either live or inactivated BoHV-1 strain while marker vaccines are gene deleted type mutants. Glycoprotein E, thymidine kinase (tk) gene or both, nonessential genes for virus replication, are targets of deletion from BoHV-1 virus and are well suited for DIVA. A double-gene deleted (gE^- and tk^-) Bovine Herpes Virus type 1 vaccine is commercially available (van Engelenburg et al., 1994). These vaccines are effective in preventing clinical disease and reducing virus transmission but are not able to prevent infection from field virus. Most of the European countries have banned the use of conventional live vaccine and are strictly using marker vaccines for effective protection and serosurveillance with the aim of disease eradication. Majority of these vaccines are licensed for immunization of pregnant animals. Most of these vaccines are licensed for use in the United States or European countries and manufactured by Zoetis UK, MSD Animal Health and Laboratorios Hipra, Spain.

20.5.2.10 Influenza (flu)

Influenza in domestic animals is caused by members of genus influenza virus A and most of have a zoonotic impact worldwide. Influenza virus A infects bird (both domestic and wild), pig, horse, dog, seal, whales, including human (Webster et al., 1992). Avian influenza, swine influenza, equine influenza, and canine influenza are the most common types of influenza virus A infection in birds, pigs, equines, and canines, respectively (Webster et al., 1992; Yoo et al., 2018). At present 16 hemagglutinin (HA) and 9 neuraminidase (NA) subtypes have been recognized, while 2 additional HA and NA subtypes have been identified in bats and these subtypes can form thousands of antigenic combination (Gamblin and Skehel, 2010; Ciminski et al., 2017). Influenza virus A subtypes; H7N7and H3N8 cause respiratory disease in horses, H1N1, H1N2 and H3N8 cause influenza in swine, H3N8 and H3N2 cause respiratory implications in dogs (Yoo et al., 2018). Generally, all genetic combinations are reported from the domestic or wild bird that causes respiratory and systemic implication, but detection of H5 and H7 are prime importance due to their high virulence (Harfoot and Webby, 2017). In humans historically endemic H1N1, H2N2, H3N2, and more recently sporadic or limited H5N1, H7N3, H7N7, and H9N2 viruses caused respiratory diseases while H3N2 and H1N1 are currently circulating subtypes (Yoo et al., 2018). Avian influenza on the basis of the presence of single or several basic amino acids at the cleavage site in haemagglutinin are classified into low pathogenicity avian influenza (LPAI) and highly pathogenicity avian influenza (HPAI) virus (Lee et al., 2004). Both types affect different avian species but wild and migratory birds act as a reservoir of LPAI. OIE has defined avian influenza as "an infection of poultry caused by any influenza A virus with HPAI and by H5 and H7 subtypes with low pathogenicity (H5/H7 LPAI)." Affected birds exhibit varying clinical manifestations from mild to severe respiratory, nervous, gastrointestinal, and reproductive system disease and sometimes birds are dead without any clinical appearance (Horby, 2014). Further, LPAI viruses also cause a considerable loss due to anorexia, respiratory signs, reduce egg production, and less weight gain. OIE recommended eradication of HPAI virus from poultry due to severe economic consequences in poultry industries in terms of reduced egg production, low quality of eggs, mortality, and evolution of new antigenic mutants via antigenic shift and drift posing a threat to humans. In addition to the controlled elimination of infected poultry, strict biosecurity, restriction on movement and purchase of birds, and good hygiene in the poultry farm, vaccination of birds is also followed. Currently inactivated mono and bivalent vaccines having H5 and H7 strains and live recombinant vaccines (fowlpox-H5) are available for immunization of poultry (Swayne, 2012). The reverse genetic-based recombinant H5N1 vaccine was also evaluated in mice and found to be a promising candidate vaccine against HPAI in poultry (Sedova et al., 2012; Lee and Song, 2013).

Swine influenza is another economically important disease caused by *influenza virus A* and affects the pork industry due to the significant reduction in

growth rate and public health misperception about eating of pork. Besides, H1N1 is the most common flu which affects humans worldwide and causes mortality. Good management practices in swine farming and use of vaccines can limit the swine influenza and consequently the possibility of human transmission. Most of the available licensed vaccines have inactivated whole virus of H1 or H3 subtypes. For immunization of pigs bivalent vaccine having H1N1 and H3N2 are used through *I/M* route and are protective to antigenically identical or similar strains. Recently intranasal poly I: C adjuvanted vaccine was found more protective compared to conventional vaccines (Kim et al., 2015). Further polyvalent vaccines containing multiple H1 and H3 clusters were commercialized with the goal of protection from new emerging antigenic cluster within subtypes of H1 and H3 (MaxiVac Excell 5.0, Merck Animal Health, Summit, NJ, USA; FluSure XP, Zoetis, Florham Park, NJ, USA). New generation vaccines based on reverse genetic strategy to make attenuated- live vaccine, DNA vaccine, subunit vaccine, and vectored = based vaccine were also evaluated experimentally for immunization of pigs but only alphavirus-like replicon particles (RP) having gene encoding the HA of a cluster IV H3N2 virus was licensed for pig use ("Swine Influenza Vaccine, RNA"; Harris vaccines, Ames, IA, USA) (Abente et al., 2019).

Equine influenza, a highly contagious respiratory disease of equine characterized with high temperature, nasal discharge, coughing, with high morbidity, and occasional mortality in foal and donkeys is one of most important infectious respiratory disease of equine worldwide. The disease has an impact on racing horse industries and tourism in hilly tracts due to inability to move. Besides, equine influenza is known to infect humans and dogs, and have the potential to generate pandemic virus. Vaccination is the most effective strategy in addition to isolation, restriction in movement, biosecurity measures to prevent disease, and its consequence on public health. Three different types; inactivated whole virus/ subunit-ISCOM-matrix or ISCOM, live- attenuated and vector-based equine influenza vaccines are available commercially (Dilai et al., 2018). The currently licensed inactivated vaccines contain H3N8 and H7N7 strains while live- attenuated vaccines have cold-adopted H3N8 strain. Subunit vaccines have either HA or both HA and NA proteins formulated with a suitable adjuvant. Canary pox virus vector is used for expression of HA gene expression after injection in the host. Currently inactivated and recombinant vaccines are used most frequently for immunization of horses.

20.5.2.11 Winter dysentery

Winter dysentery is an infectious and contagious gastroenteric disorder of adult cattle, often reported in winter season characterized by profuse watery diarrhea with fresh blood, significant loss in milk production, and disturbs health conditions. The causative agent of this highly morbid disease is bovine coronavirus (BCoV) (Saif, 1990). In addition to gastric infection, BCoV also affects the respiratory system of calves and feedlot cattle. The disease on sets is sudden and within a few days, most of the animals of the herd suffer from diarrhea. Milk

production may not return to full capacity even after a long time of animal recovery or of that lactation. Due to rapid onset, high morbidity, and huge reduction in milk loss the disease is worrisome to dairy industries and farmers. For prevention of winter dysentery, there is no dedicated vaccine. However MLV coronavirus vaccine (BOVILIS Coronavirus, Intervet/Merck Animal Health) which is recommended for calves' diarrhea caused by bovine coronavirus. Further, a solubilized antigen from BCoV-infected cells combined with an oil adjuvant was tested as a prototype vaccine to be used against winter dysentery (Takamura et al., 2000, 2002).

20.5.2.12 Rotavirus gastroenteritis

Rotaviruses (RV) affect young ones of cattle, pigs, sheep, goats, horses, and poultry, including humans. It is one of the major concerns of neonatal diarrhea in domestic animals and mostly caused by group A RV (total 9 group A−I). Bovine rotavirus (BRV) affects calves of 2−8 weeks of age and its susceptibility decreases as age progresses. Clinical manifestation in each species is similar ranging from asymptomatic subclinical condition to severe enteritis. Clinically calves suffer from acute, watery, dehydrating diarrhea and may succumb to infection. The morbidity and mortality are very high, leading to huge economical losses in dairy and beef industries worldwide. Mucosal immunity plays a major role to inhibit intestinal infections by any infectious pathogen and it is transferred from the dam to new young ones via colostrum feeding. Therefore if the pregnant dam is immunized with a rotavirus vaccine sufficiently, she can transfer antirotavirus maternal antibodies in surplus to protect calves sufficiently long duration. Both conventional and new generation vaccine such as subunit, DNA vaccine, VLP, plant-based edible vaccine (used VP-4, VP-6, or capsid protein), reverse genetic-based vaccine and recombinant BCG expressing VP-6 gene were evaluated to generate protective immunity (Poelaert et al., 2018; Chen et al., 2012). Commercially attenuated strains of BRV and coronavirus (Galf Guard, Zoetis, USA, PBS animal health, United States) are used to immunize calves and adult cattle. Inactivated BRV (serotypes G6 and G10) and coronavirus propagated on established cell lines and a K99 *E. coli* bacterin formulated with adjuvant (scourGuard, Zoetis, USA, MSD animal health) are used to immunize pregnant cattle and heifers. Further, some vaccines have *Clostridium perfringens* type C and type D toxoid, *E. coli* K99 along with inactivated bovine coronavirus type 1 and 3, inactivated BRV type G6 and G10 (Cooper).

20.5.2.13 Parasitic vaccines

Livestock is susceptible for so many parasitic infestations such as nematodes, protozoa, and insects. The parasitic infestations lead to poor animal's performance and their productions. For the control of parasites, different antimicrobials are available but due to the evolution of antimicrobials resistance, they are becoming ineffective against most of the parasites. Further, various vaccination strategies were also employed to develop parasitic vaccines but very few vaccines are

commercially available for immunization, probably due to difficulties in vaccines development, poor immune responses, and very high cost of production. The vaccines which are used for immunization of livestock are described here.

20.5.2.14 Theileriosis

A tick-born apicomplexan parasitic disease affects domestic and wild ruminant worldwide. The disease is caused by *Theileria* species, most notably *T. parva* and *T. annulata* in cattle and *T. lestoquardi* in sheep. Transmission of *T. parva* and *T. annulata* are through *Rhipicephalus appendiculatus* ticks, occurs in eastern and southern Africa, and by *Hyalomma* ticks, occurs around the Mediterranean basin, north-east Africa, the Middle East, India, and southern Asia, respectively. African buffalo and Asian buffalo are also susceptible to *T. parva* and *T. annulata*, respectively. *Theileria* species cause acute lymphoproliferative disease with a high level of morbidity and mortality and economic losses (Sivakumar et al., 2014). For control of the disease, acaricides and buparvaquone (therapeutic compound) are used but due to regular use of acaricides and the high cost of buparvaquone, the overall control and treatment are very expensive. Besides, drug resistant *T. annulata* is also reported recently. Vaccination is the only sustainable alternative of these limitations (Nene and Morrison, 2016). Immunization with *T. parva* and *T. annulata* infected cell line as live vaccines were attempted but found to be noneconomical. A live vaccine having infectious sporozoites was developed. Because of limitations in live vaccines, other alternatives were searched to develop subunit and viral-vectored vaccines based on the use of defined antigens of sporozoite (Knight et al., 1996) and schizont (Goh et al., 2016) developmental stages. But at present only live vaccines against both *T. parva* and *T. annulata* based on sporozoites are used to immunize the animals.

20.5.2.15 Coccidiosis

Avian coccidiosis is responsible for huge economic losses in the poultry sector incurred by parasitic diseases and is caused by different *Eimeria* species. Among them, *Eimeria tenella* is the most pathogenic one and can develop resistance rapidly against anticoccidial drugs. For control of coccidia in poultry farm, prophylactic use of anticoccidial drugs were followed since long and still are the preferred method. But the problem is the quick development of resistance against available anticoccidial drugs and requirement of new drugs. In addition to chemotherapy, vaccination is also used to protect chickens (Tewari and Maharana, 2011). Most commonly used vaccines for immunization of chickens are live oocysts either from attenuated or nonattenuated strains of coccidian (Chapman and Jeffers, 2014). Nonattenuated live vaccines have variable numbers of wild coccidian strains depending upon their use in broiler breeders (up to eight strains, Coccivac-D, and Immucox-C2), or broiler industries (up to four strains Coccivac-B, Immucox-C1) but the main risk is development of severe reaction in vaccinated poultry. The live-attenuated oocysts vaccine strains (Paracox and HatchPak CocciIII) have fewer vaccines-induced risks (Price, 2012). Indigenous live-attenuated

quadrivalent coccidia vaccine having *Eimeria tenella, E. acervulina, E. maxima*, and *E. necatrix* (LivacoxQ, Hester) is available in India. DNA recombinant technology was also used to develop a recombinant vaccine based on an immunodominant portion of proteins of various stages either of sporozoites or merozoites or gametes of *Eimeria* species (Tewari and Maharana, 2011). At present only one commercialized subunit vaccine is available for coccidiosis (CoxAbic) based on purified native protein extracted from gametocytes of *Eimeria*.

20.5.2.16 Parasitic bronchitis
Parasitic bronchitis is primarily a disease of cattle caused by *D. viviparous* which is also called lung worm. The disease is characterized with extension of neck, open mouth breathing, and coughing which is consider as "hoose or husk." Morbidity is high but mortality is less and in less severely affected animals recover by self-cure phenomenon after several months. For control of lung worm anthelmintic drugs and prophylactic vaccines are used. Prophylactic vaccination is done by commercially-available live-attenuated vaccine incorporated with gamma irradiated third stage larva (L3). Though this vaccine is used successfully in different developed countries, it has some limitations such short shelf-life, requirement of booster, and high cost. Recently, a recombinant subunit vaccine based on parasites' muscle protein paramyosin expressed in *E. coli* was evaluated to control lung worm burden in cattle in comparison to irradiated *D. viviparous* vaccine (Bovilis Dictol live vaccine) and found to be a promising strategy to develop recombinant vaccine against lungworm infestation in cattle.

20.6 Combined vaccination
Inoculation of more than one vaccine by single shot is called combined vaccination. The first combined vaccination was done since long back in 1948 to vaccinate infants with combination of diphtheria, tetanus, and pertusis (DPT) vaccines in a single shot. Inoculation of multiple vaccines in single volume at a time reduces the multiple injections, time to vaccinate the animals, suffering of animals, cost and visit of veterinarian. It provides protection against multiple pathogens simultaneously and minimizes chances of missing vaccination schedule and time. There are so many available combined vaccines for companion and domesticated animals. For vaccination of pups core vaccine; canine parvovirus, canine distemper virus, canine adenovirus, canine parainfluenza, canine corona virus, rabies, and leptospira are given in combined form by single shot. Bovine respiratory syncytial virus, bovine viral diarrhea virus types 1 and 2 and *Mannheimia haemolytica* are inoculated simultaneously in cattle or buffalo while sheep pox either with PPRV or bluetongue vaccines are used for vaccination of sheep (Table 20.2).

Table 20.2 Recommended vaccines for cattle.

Name of disease	Age at first dose	Booster dose	Subsequent dose
Foot and mouth disease (FMD)	4 months and above	1 month after first dose	Six monthly
Hemorrhagic septicemia	6 months and above		Annually in endemic areas
Black quarter (BQ)	6 months and above		Annually in endemic areas
Brucellosis	4−8 months of age (only female calves)		Once in a lifetime
Theileriosis	3 months of age and above		Once in a lifetime. Only required for crossbred animals
Anthrax	4 months and above		Annually in endemic areas
IBR	3 months and above	1 month after first dose	Six monthly
Rabies (post bite therapy)	Immediately after suspected bite	Fourth day	7, 14, 28, and 90 (optional) days after first dose

20.7 Poultry vaccines

The poultry market is the biggest market in livestock sectors, as poultry farming such as chickens require less time to attain marketable age, produce nearly one egg each day, and require less investment. Chickens are reared mainly for broiler (meat) and layer (eggs) purposes. Along with nutritional and housing management, good health is of paramount importance to achieve better growth rates in broilers and to get good quality eggs from layers throughout year. Poultry are susceptible to many infectious diseases such as infectious bursal disease, infectious bronchitis, infectious laryngotracheitis, Marek's disease, Newcastle disease, Fowl pox, avian influenza, fowl cholera, fowl typhoid, bacillary white diarrhea, chronic respiratory disease, and coccidiosis, etc. (Deshmukh et al., 2015; Jordan, 2017; García, 2017; Yuan et al., 2018; Alkie and Rautenschlein, 2016; Wua et al., 2011; Reddy et al., 2016). Morbidity and mortality caused by the pathogens are very high leading to negative impact on production and human welfare due to shortage of food supply. These diseases could be controlled by immunization of poultry flocks with negligible expense on each bird. For immunization of poultry conventional (inactivated and live) and biotechnological or genetic engineering (subunit, vectored, DNA, and VLP) tools have been employed to develop effective vaccines. But, availability of recombinant (biotechnological based) vaccines for field use are very limited as most of them are in different phases of clinical trials or have some quality control issues. At present either inactivated or

live-attenuated vaccines are being used for mass immunization of poultry flocks. The susceptibility toward different diseases depends on the age of birds. Therefore two types of vaccination schedule are recommended for poultry flocks, namely for boilers and layers (Table 20.3).

Table 20.3 Commercialized and candidate vaccines for poultry.

Pathogens	Inactivated	Live	Recombinant
Newcastle disease	Different strains such mesogenic (R2b,) and lentogenic (Lasota, B1, F) are used after chemical inactivation	Attenuated strains such mesogenic (R2b,) and lentogenic (Lasota, B1, F)	*Vectored vaccine* 1 Fowl pox vectored vaccine expressing hemagglutinin-neuraminidase (HN) or F gene 2 Herpes virus of turkey expressing F gene 3 Recombinant Marek's disease virus vaccine of serotype 1 (Rispens strain) expressing the protein encoded by the VP2 gene of IBDV with a rHVT-ND 4 Recombinant Infectious bursal disease virus (IBDV) containing the HN of NDV
Infectious bronchitis	Formaldehyde inactivated Massachusetts (Mass) serotype IBV (most common) and other serotypes such as; Arkansas (Ark), Connecticut (Conn), Delaware (Del), Georgia98 (GA98), Georgia 08 (GA08), and Georgia 13 (GA13)	Massachusetts (Mass) serotype IBV by serial passage or both passage and mild heat treatment	*Vectored vaccine* 1 HVT and Fowl pox virus encoding S-1 gene 2 Viral backbones, such as NDV, duck enteritis virus, and avian metapneumovirus encoding S-1 and S-2 *Recombinant live virus* Reverse genetic-based recombinant virus coding spike gene from avirulent virus

(*Continued*)

Table 20.3 Commercialized and candidate vaccines for poultry. *Continued*

Pathogens	Inactivated	Live	Recombinant
Infectious laryngotracheitis		Chicken embryo origin (CEO) SA2, A20 and tissue culture origin (TCO) GaHV-1 vaccines	*Vectored vaccine* 1 FPV vector having the GaHV-1 glycoprotein B and UL32 genes 2 HVT vector coding GaHV-1 glycoproteins I, B, and D 3 Bivalent HVT or FPV vaccine for GaHV-1 and MD 4 LaSota strain expressing GaHV-1 glycoproteins vaccine 5 Modified very virulent (vv) serotype I Marek disease virus (MDV) expressing GaHV-1 glycoproteins
Infectious bursal disease		Mild, intermediate, or intermediate plus strains	*Vector vaccine* 1 Fowl pox and Marek's disease vector vaccine expressing VP-2 gene 2 Bacterial delivery VP-2 gene of IBDV by *Salmonella typhimurium* *Subunit vaccine* 1 Hypervariable region of VP-2 expressed in *Pichia pastoris* or *E. coli* *DNA vaccine* Immunodominant VP2 gene fragment (VP252−417), VP2 and HSP70 (fused and expressed in one plasmid),

(Continued)

Table 20.3 Commercialized and candidate vaccines for poultry. *Continued*

Pathogens	Inactivated	Live	Recombinant
Marek's disease		*Serotype 3 vaccines*: *MDV-3:* most commonly used strain is FC126.	**Vectored vaccine** 1 FPV expressing MDV1-gB
		Serotype 2 vaccines: *MDV-2:* CVI988 strain or Rispens (most efficient vaccine)	*MDV-1 Gene deletion vaccines*: MD virus having pp38 deletion, or vIL8 deletion or vTR deletion/mutation or Meq deletion (ΔMeq)
		Serotype 1 vaccines: *MDV-1:* HPRS-16/att	
Infectious coryza	Whole cell *Avibacterium paragallinarum* serovars A-1, B-1, C-1, or C-2 killed with thimerosal or formalin (most widely used)	Live-attenuated strains of *A. paragallinarum* serovars A-1, B-1, C-1, or C-2	*Subunit vaccine* Hypervariable region in the HA proteins of *A. paragallinarum* serovars A and C expressed in *E. coli*
Salmonella	Inactivated whole cell *S*. Enteritidis	Live-attenuated mutant or gene-deleted salmonella Such *Salmonella* Enteritidis ΔaroA,	*Subunit vaccine*: *S*. Enteritidis protein extract or protein, FliC, Type I fimbriae and SPI-1 and SPI-2 proteins
			DNA vaccine: Bacterial plasmid encoding SopB, a Salmonella SPI-1 effector protein
		S. typhimurium Δcya/crp, Ts *S.* Enteritidis mutant, *S.* Enteritidis ΔphoP/fliC	*Vectored vaccine*: Live-attenuated *Salmonella* itself acts as vector for delivery of other antigen and induce immunity against itself
Fowl cholera	Killed serotypes A-1, A-3, and A-4 of *Pasteurella multocida* strain	Live-attenuated serotype of *P. multocida*	*Subunit vaccine* Outer membrane protein H (rOmpH) expressed in *E. coli*

20.8 Adverse effect of vaccines

Though, vaccines are considered excellent in preventing infectious diseases, they have some adverse effects on the host. Adverse effects caused by vaccines may be transient or for longer duration and can be caused either by antigens or adjuvants present in vaccines. Generally the side reaction is associated with live vaccine but killed vaccine also in some cases can cause a reaction. Latent infections can be caused by a certain vaccine virus, that is, herpesvirus vaccines. In some cases animal may fail to respond to vaccine or it may be excreting vaccine virus or bacteria in their secretion and excretion such as BVDV and *Brucella* vaccines. Sometimes MLV BTV vaccines regain virulence inside the host/vectors leading to development of clinical manifestations and raising the concern about possibilities of genetic assortment between vaccine and wild viruses. Feline leukemia virus vaccine at the injection site in leg causes development of a lump which regresses within few days but sometimes cats suffer with a lethal cancerous condition called fibrosarcoma. Rabies vaccines also lead fibrosarcoma development at inoculation site in cats similar to feline leukemia vaccines. Other common side effects include: transient swelling at the site of injection, coughing, fever, anaphylaxis, respiratory distress, salivation, vomiting, diarrhea, urticaria, reduced fertility, abortion, and fetal abnormalities.

No doubt some vaccines have adverse effects but overall advantages of vaccination outweight the adverse effects. Immunizations of livestock against different infectious agents are playing a pivotal role in keeping animals healthy, sustaining animal production and food security. This is only due to vaccination, the world has become free from two dreaded diseases such as small pox of human beings and rinderpest of cattle. Besides, some other infectious diseases also has been eradicated from different countries such as African horse sickness, FMD, swine vesicular disease, and rabies, etc., and many more are in the line of eradication.

References

Abente, E.J., Rajao, D.S., Gauger, P.C., Vincent, A.L., 2019. Alphavirus-vectored hemagglutinin subunit vaccine provides partial protection against heterologous challenge in pigs. Vaccine 37 (11), 1533−1539.

Abreu, C.C., Edwards, E.E., Edwards, J.F., Gibbons, P.M., Araújo, J.L., Rech, R.R., et al., 2017. Blackleg in cattle: a case report of fetal infection and a literature review. J. Vet. Diag. Invest. 29 (5), 612−621.

Adem, J., Bushra, E., 2016. Bovine salmonellosis and its public health importance: a review. Adv. Life Sci. Technol. 44, 62−71.

Alkie, T.N., Rautenschlein, S., 2016. Infectious bursal disease virus in poultry: current status and future prospects. Vet. Med. Res. Rep. 7, 9−18.

Arimitsu, H., Lee, J.C., Sakaguchi, Y., Hayakawa, Y., Hayashi, M., Nakaura, M., et al., 2004. Vaccination with recombinant whole heavy chain fragments of *Clostridium botulinum* Type C and D neurotoxins. Clin. Diag. Lab. Immunol. 11 (3), 496−502.

Balseiro, A., Altuzarra, R., Vidal, E., Moll, X., Espada, Y., Sevilla, I.A., et al., 2017. Assessment of BCG and inactivated *Mycobacterium bovis* vaccines in an experimental tuberculosis infection model in sheep. PLoS One 12 (7), e0180546. Available from: https://doi.org/10.1371/journal.pone.0180546.

Basu, A., Dutta, K., 2017. Recent advances in Japanese encephalitis. F1000Res. 6, 259. Available from: https://doi.org/10.12688/f1000research.9561.1. eCollection 2017.

Beer, M., Hehnen, H.R., Wolfmeyer, A., Poll, G., Kaaden, O.R., Wolf, G., 2000. A new inactivated BVDV genotype I and II vaccine. An immunisation and challenge study with BVDV genotype I. Vet. Microbiol. 77, 195−208.

Bhanuprakash, V., Indrani, B.K., Hosamani, M., Balamurugan, V., Singh, R.K., 2009. Bluetongue vaccine: the past present and future. Expert Rev. 8, 191−204.

Bhanuprakash, V., Hosamani, M., Singh, R.K., 2011. Prospects of control and eradication of capripox from the Indian subcontinent: a perspective. Antiviral Res. 91 (3), 225−232. Available from: https://doi.org/10.1016/j.antiviral.2011.06.004.

Bhanuprakash, V., Hosamani, M., Venkatesan, G., Balamurugan, V., Yogisharadhya, R., Singh, R.K., 2012. Animal poxvirus vaccines: a comprehensive review. Expert Rev. Vaccines 11, 1355−1374.

Bharti, A.R., Nally, J.E., Ricaldi, J.N., Matthias, M.A., Diaz, M.M., Lovett, M.A., et al., 2003. Leptospirosis: a zoonotic disease of global importance. Lancet Infect. Dis. 3, 757−771.

Blanton, J.D., Kis Robertson, M.P.H., Palmer, D., Rupprecht, C.E., 2009. Rabies surveillance in the United States during 2008. J. Am. Vet. Med. Assoc. 235 (6), 676−689.

Blome, S., Staubach, C., Henke, J., Carlson, J., Beer, M., 2017. Classical swine fever—an updated review. Viruses 9 (4), E86. Available from: https://doi.org/10.3390/v9040086.

Bolin, C.A., Cassells, J.A., Zuerner, R.L., Trueba, G., 1991. Effect ofvaccination with a monovalent *Leptospira interrogans* serovar hardjo type hardjo−bovis vaccine on type Hardjo−Bovis infection of cattle. Am. J. Vet. Res. 52, 1639−1643.

Boumart, Z., Daouam, S., Belkourati, I., Rafi, L., Tuppurainen, E., Tadlaoui, K.O., et al., 2016. Comparative innocuity and efficacy of live and inactivated sheeppox vaccines. BMC Vet. Res. 12 (1), 133. Available from: https://doi.org/10.1186/s12917-016-0754-0.

Buttigieg, M., 2015. A review of the one health concept: increasing awareness and collaboration between the Maltese medical and veterinary professionals. Malta Med. J. 27 (05), 34−37.

Chand, K., Biswas, S.K., Pandey, A.B., Muthuchelvan, D., Mondal, B., 2015. Bluetongue in India: a review. Adv. Anim. Vet Sci. 3 (11), 605−612.

Chapman, H.D., Jeffers, T.K., 2014. Vaccination of chickens against coccidiosis ameliorates drug resistance in commercial poultry production. Int. J. Parasitol.: Drugs Drug Resist. 4, 214−217.

Chawla, A., Midha, S., Bhatnagar, R., 2009. Efficacy of recombinant anthrax vaccine against *Bacillus anthracis* aerosol spore challenge: preclinical evaluation in rabbits and Rhesus monkeys. Biotechnol. J. 3, 391−399. Available from: https://doi.org/10.1002/biot.200800213.

Chen, S., Tan, L., Huang, L., Chen, K., 2012. Rotavirus infection and the current status of rotavirus vaccines. J. Formos. Med. Assoc. 111, 183−193.

Ciminski, K., Thamamongood, T., Zimmer, G., Schwemmle, M., 2017. Novel insights into bat influenza A viruses. J. Gen. Virol. 98 (10), 2393−2400.

Corbel, M.J., 2006. Brucellosis in Humans and Animals. WHO Publishing, Geneva.

Cousins, D.V., 2001. *Mycobacterium bovis* infection and control in domestic livestock. Rev. Sci. Tech. 20, 71−85.

Cullen, P.A., Cordwell, S.J., Bulach, D.M., Haake, D.A., Adler, B., 2002. Global analysis of outer membrane proteins from *Leptospira interrogans* serovar Lai. Infect. Immun. 70, 2311−2318.

Danielle, A.B., 2006. Deadly diseases and epidemics: *Salmonella*. In: Heymann, David (Ed.), Communicable Diseases Section. World Health Organization, Geneva, pp. 8−74. Chelsea House Publishers.

De Alwis, M.C.L., 1992. Haemorrhagic septicaemia—a general review. Br. Vet. J. 148, 99−112.

Deshmukh, S., Banga, H.S., Sodhi, S., Brar, R.S., 2015. An update on avian infectious coryza: its re-emerging trends on epidemiology, etiologic characterization, diagnostics, therapeutic and prophylactic advancements. J. Dairy Vet. Anim. Res. 2 (3), 86−92. Available from: https://doi.org/10.15406/jdvar.2015.02.00037.

Diallo, A., Taylor, W.P., Lefèvre, P.C., Provost, A., 1989. Attenuation of a strain of rinderpest virus: potential homologous live vaccine. Rev. élev. Méd. Vét. Pays Trop. 42 (3), 311−319.

Diallo, A., Minet, C., Le Goff, C., Berhe, G., Albina, E., Libeau, G., et al., 2007. The threat of peste des petits ruminants: progress in vaccine development for disease control. Vaccine 25 (30), 5591−5597. Available from: http://dx.doi.org/10.1016/j.vaccine.2007.02.013.

Dilai, M., Piro, M., Harrak, M.E., Fougerolle, S., Dehhaoui, M., Dikrallah, A., et al., 2018. Impact of mixed equine influenza vaccination on correlate of protection in horses. Vaccines (Basel) 6 (4), 71.

Duncan, J., Maskell, K.J., Sweeney, D.C.E., Hormaeche, F.Y., Liew, G.D., 1987. *Salmonella typhimuriumaro* A mutants as carriers of the *Escherichia coli* heat-labile enterotoxin B subunit to the murine secretory and systemic immune systems. Microb. Pathog. 2 (3), 211−221.

Eblé, P.L., Quak, S., Geurts, Y., Moonen-Leusen, H.W., Loeffen, W.L., 2014a. Efficacy of CSF vaccine CP7_E2alf in piglets with maternally derived antibodies. Virus Res. 179, 1−11.

Eblé, P.L., Geurts, Y., Quak, S., Moonen-Leusen, H.W., Blome, S., Hofmann, M.A., et al., 2014b. Efficacy of chimeric Pestivirus vaccine candidates against classical swine fever: protection and DIVA characteristics. Vet. Microbiol. 174 (1-2), 27−38.

Edelman, R., Russell, R.G., Losonsky, G., Tall, B.D., Tacket, C.O., Levine, M.M., et al., 1993. Immunization of rabbits with enterotoxigenic *E. coli* colonization factor antigen (CFA/I) encapsulated in biodegradable microspheres of poly (lactide-co-glycolide). Vaccine 11 (2), 155−158.

Faine, S., Adler, B., Bolin, C., Perolat, P., 1999. Leptospira and Leptospirosis, second ed. Medisci, Melbourne.

Fox, J.T., Thomson, D.U., Drouillard, J.S., Thornton, A.B., Burkhardt, D.T., Emery, D.A., et al., 2009. Efficacy of *Escherichia coli* O157:H7 siderophore receptor/porin proteins-based vaccine in feedlot cattle naturally shedding *E. coli* O157. Food Borne Pathog. Dis. 6 (7), 893−899. Available from: https://doi.org/10.1089/fpd.2009.0336.

Frey, J., Falquet, L., 2015. Patho-genetics of *Clostridium chauvoei*. Res. Microbiol. 166, 384−392.

Gamblin, S.J., Skehel, J.J., 2010. Influenza hemagglutinin and neuraminidase membrane glycoproteins. J. Biol. Chem. 285 (37), 28403−28409.

García, M., 2017. Current and future vaccines and vaccination strategies against infectious laryngotracheitis (ILT) respiratory disease of poultry. Vet. Microbiol. 206, 157−162.

Gilardoni, L.R., Paolicchi, F.A., Mundo, S.L., 2012. Bovine paratuberculosis: a review of the advantages and disadvantages of different diagnostic tests. Rev. Argent. Mirobiol. 44 (3), 201−215.

Goh, S., Ngugi, D., Lizundia, R., et al., 2016. Identification of *Theileria lestoquardi* antigens recognized by CD8$^+$T cells. PLoS One 11, e0162571.

Golshani, M., Buozari, S., 2017. A review of brucellosis in Iran: epidemiology, risk factors, diagnosis, control, and prevention. Iran Biomed. J. 21 (6), 349−359.

Grabenstein, J.D., 2003. Anthrax vaccine: a review. Immunol. Allergy Clin. N. Am. 23 (4), 713−730.

Grang, J.M., 2001. *Mycobacterium bovis* infection in human beings. Tuberculosis 81 (1−2), 71−77.

Grubman, M.J., Baxt, B., 2004. Foot-and-mouth disease. Clin. Microbiol. Rev. 12, 465−493.

Harfoot, R., Webby, R.J., 2017. H5 influenza, a global update. J. Microbiol. 55 (3), 196−203.

Hebbelstrup Jensen, B., Olsen, K.E., Struve, C., Krogfelt, K.A., Petersen, A.M., 2014. Epidemiology and clinical manifestations of enteroaggregative *Escherichia coli*. Clin. Microbiol. Rev. 27 (3), 614−630.

Hodgson, J.C., Finucane, A., Dagleish, M.P., Ataei, S., Parton, R., Coote, J.G., 2005. Efficacy of vaccination of calves against hemorrhagic septicemia with a live aroA derivative of Pasteurella multocida B:2 by two different routes of administration. Infect. Immun. 73 (3), 1475−1481. Available from: https://doi.org/10.1128/IAI.73.3.1475-1481.2005.

Hoelzer, K., Bielke, L., Blake, D.P., Cox, E., Cutting, S.M., Bert, D., et al., 2018. Vaccines as alternatives to antibiotics for food producing animals. Part 2: new approaches and potential solutions. Vet. Res. 49, 70. Available from: https://doi.org/10.1186/s13567-018-0561-7.

Horby, P.W., 2014. Community studies of influenza: new knowledge, new questions. Lancet Respir. Med. 2 (6), 430−431.

Huang, Y.L., Deng, M.C., Wang, F.I., Huang, C.C., Chang, C.Y., 2014. The challenges of classical swine fever control: modified live and E2 subunit vaccines. Virus Res. 179, 1−11.

Jamal, S.M., Belsham, G.J., 2013. Foot-and-mouth disease: past, present and future. Vet. Res. 44, 116−130.

Janewongwirot, P., Puthanakit, T., Anugulruengkitt, S., et al., 2016. Immunogenicity of a Japanese encephalitis chimeric virus vaccine as a booster dose after primary vaccination with SA14-14-2 vaccine in Thai children. Vaccine 34 (44), 5279−5283.

Jennings, G.T., Bachmann, M.F., 2008. The coming of age of virus-like particle vaccines. Biol. Chem. 389 (5), 521−536. Available from: https://doi.org/10.1515/BC.2008.064.

Jordan, B., 2017. Vaccination against infectious bronchitis virus: a continuous challenge. Vet. Microbiol. 206, 137−143. Available from: https://doi.org/10.1016/j.vetmic.2017.01.002.

Jorge, S., Dellagostin, O.A., 2017. The development of veterinary vaccines: a review of traditional methods and modern biotechnology approaches. Biotechnol. Res. Innov. 1, 6−13.

Kaur, M., Singh, S., Bhatnagar, R., 2013. Anthrax vaccines: present status and future prospects. Expert Rev. Vaccines 12 (8), 955−970.

Kemal, J., 2014. A review on the public health importance of bovine salmonellosis. J. Vet. Sci. Technol. 5, 175. Available from: https://doi.org/10.4172/2157-7579.1000175.

Khare, S., Alali, W., Zhang, S., Hunter, D., Pugh, R., Fang, F.C., et al., 2010. Vaccination with attenuated *Salmonella enterica* Dublin expressing *E. coli* O157:H7 outer membrane protein Intimin induces transient reduction of fecal shedding of *E. coli* O157:H7 in cattle. BMC Vet. Rese. 7 (6), 35. Available from: https://doi.org/10.1186/1746-6148-6-3.

Kim, E., Han, S.J., Byun, Y.H., Yoon, S.C., Choi, K.S., Seong, B.L., et al., 2015. Inactivated eyedrop influenza vaccine adjuvanted with poly(I:C) Is safe and effective for inducing protective systemic and mucosal immunity. PLoS One 10 (9), e0137608.

Knight, P., Musoke, A.J., Gachanja, J.N., et al., 1996. Conservation of neutralizing determinants between the sporozoite surface antigens of *Theileria annulata* and *Theileria parva*. Exp. Parasitol. 82, 229−241.

Lee, D.H., Song, C.S., 2013. H9N2 avian influenza virus in Korea: evolution and vaccination. Clin. Exp. Vaccine Res. 2 (1), 26−33.

Lee, C.W., Senne, D.A., Linares, J.A., Woolcock, P.R., Stallknecht, D.E., Spackman, E., et al., 2004. Characterization of recent H5 subtype avian influenza viruses from US poultry. Avian Pathol. 33 (3), 288−297.

Levett, P.N., 2001. Leptospirosis. Clin. Microbiol. Rev. 14, 296−326.

Lindahl, J.F., Stahl, K., Chirico, J., Boqvist, S., Thu, H.T.V., et al., 2013. Circulation of Japanese encephalitis virus in pigs and mosquito vectors within Can Tho City, Vietnam. PLoS Negl. Trop. Dis. 7 (4), e2153. Available from: https://doi.org/10.1371/journal.pntd.0002153.

Lokhandwala, S., Fang, X., Waghela, S.D., Bray, J., Njongmeta, L.M., Herring, A., et al., 2017. Priming cross-protective bovine viral diarrhea virus-specific immunity using live-vectored mosaic antigens. PLoS One 12 (1), e0170425. Available from: https://doi.org/10.1371/journal.pone.0170425.

Madhavan, A., Venkatesan, G., Kumar, A., 2016. Capripoxvirus of small ruminants: current updates and future perspective. Asian J. Anim. Vet. Adv. 11, 757−770.

Mayo, C., Lee, J., Kopanke, J., MacLachlan, N.J., 2017. A review of potential bluetongue virus vaccine strategies. Vet. Microbiol. 206, 84−90.

McConnell, I., 2014. One health in the context of medical and veterinary education. Sci. Tech. Rev. 33 (2), 651−657.

McEvoy, J.M., Doherty, A.M., Sheridan, J.J., Blair, I.S., McDowell, D.A., 2003. The prevalence of *Salmonella* spp. in bovine faecal, rumen and carcass samples at a commercial abattoir. J. Appl. Microbiol. 94, 693−700.

Meeusen, E.N.T., Walker, J., Peters, A., Pastoret, P.P., Jungersen, G., 2007. Current status of veterinary vaccines. Clin. Microbiol. Rev. 20 (3), 489−510.

Moriyón, I., Grilló, M.J., Monreal, D., et al., 2004. Rough vaccines in animal brucellosis: structural and genetic basis and present status. Vet. Res. 35, 1−38.

Muller, T.F., Schuster, P., Vos, A.C., Selhorst, T., Wenzel, U.D., Neubert, A.M., 2001. Effect of maternal immunity on the immune response to oral vaccination against rabies in young foxes. Am. J. Vet. Res. 62, 1154−1158.

Muthuchelvan, D., Rajak, K.K., Ramakrishnan, M.A., Choudhary, D., Bhadouriya, S., Saravanan, P., et al., 2015. Peste-des-petits-ruminants: an Indian perspective. Adv. Anim. Vet. Sci. 3 (8), 422−429.

Myint, A., Carter, G.R., Jones, T.O., 1987. Prevention of experimental haemorrhagic septicaemia with a live vaccine. Vet. Rec. 120 (21), 500−501.

Nene, V., Morrison, W.I., 2016. Approaches to vaccination against *Theileria parva* and *Theileria annulata*. Parasite Immunol. 38 (12), 724−734.

OIE, 2017. Manual of Diagnostic Tests and Vaccinesfor Terrestrial Animals 2017. Brucellosis (*Brucella abortus*, *B. melitensis* and *B. suis*) (infection with *B. abortus*, *B. melitensis* and *B. suis*). OIE, Paris. Available from: <http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.01.04_BRUCELLOSIS.pdf>.

Palaniswami, K.S., Thangavelu, A., Velmurugan, R., 2005. Development of thermostable peste des petits ruminants (PPR) virus vaccine and assessment of molecular changes in the F gene. In: Makkar, H.P.S., Viljoen, G.J. (Eds.), Applications of Gene-Based Technologies for Improving Animal Production and Health in Developing Countries. Springer-Verlag, Berlin, pp. 673−678.

Palmer, M.V., Welsh, M.D., Hostetter, J.M., 2011. Mycobacterial diseases of animals. Veterinary Medicine International. Available from: https://doi.org/10.4061/2011/292469.

Paludan, S.R., Bowie, A.G., 2013. Immune sensing of DNA. Immunity 38, 870−880.

Pecora, A., Malacari, D.A., Pérez Aguirreburualde, M.S., Bellido, D., Escribano, J.M., Dus Santos, M.J., et al., 2015. Development of an enhanced bovine viral diarrhea virus subunit vaccine based on E2glycoprotein fused to a single chain antibody which targets to antigen-presenting cells. Rev. Argent. Microbiol. 47 (1), 4−8.

Piddock, L.J., 2002. Fluoroquinolone resistance in *Salmonella* serovars isolated from humans and food animals. FEMS Microbiol. Rev. 26, 3−16.

Plommet, M., Renoux, G., Philppon, A., Lorentz, C., Gestin, J., 1970. Brucellose experimentale. I. Comparison de l'efficacite des vaccines B19 and H38 vaccine. Ann. Rech. Vet. (Paris) 1, 189−201.

Poelaert, D., Pereira, P., Gardner, R., Standaert, B., Benninghoff, B., 2018. A review of recommendations for rotavirus vaccination in Europe: arguments for change. Vaccine 36, 2243−2253.

Poonsuk, K., Giménez-Lirola, L., Zimmerman, J.J., 2018. A review of foot-and mouth disease virus (FMDV) testing in livestock with an emphasis on the use of alternative diagnostic specimens. Anim. Health Res. Rev. 19 (2), 100−112. Available from: https://doi.org/10.1017/S1466252318000063.

Price, K.R., 2012. Use of live vaccines for coccidiosis control in replacement layer pullets. J. Appl. Poult. Res. 21, 679−692.

Ramakrishnan, M.A., Pandey, A.B., Singh, K.P., Singh, R., Nandi, S., Mehrotra, M.L., 2006. Immune responses and protective efficacy of binary ethylenimine (BEI)-inactivated bluetongue virus vaccines in sheep. Vet. Res. Commun. 30 (8), 873−880.

Rao, T.V.S., Bandyopadhyay, S.K., 2000. A comprehensive review of goat pox and sheep pox and their diagnosis. Anim. Health Res. Rev. 1, 127−136.

Reddy, Y.K.M., Manohar, B.M., Pandey, A.B., Reddy, Y.N., Prasad, G., Chauhan, R.S., 2010. Development and evaluation of inactivated pentavalent adjuvanted vaccine for Bluetongue. Indian Vet. J. 87, 434−436.

Reddy, S.M., Izumiya, Y., Lupiani, B., 2016. Marek's disease vaccines: current status, and strategies for improvement and development of vector vaccines. Vet. Microbiol. 206, 113−120.

Rizzi, C., Bianco, M.V., Blanco, F.C., Soria, M., Gravisaco, M.J., Montenegro, V., et al., 2012. Vaccination with a BCG strain overexpressing Ag85B protects cattle against *Mycobacterium bovis* challenge. PLoS One 7 (12), e51396.

Saif, L.J., 1990. A review of evidence implicating bovine coronavirus in the etiology of winter dysentery in cows: an enigma resolved? Cornell Vet. 80, 303−311.

Schurig, G.G., Sriranganathan, N., Corbel, M.J., 2002. Brucellosis vaccines: past, present and future. Vet. Microbiol. 90 (1−4), 479−496.

Sedova, E.S., Shcherbinin, D.N., Migunov, A.I., Smirnov, I.A., Logunov, D.I., Shmarov, M.M., et al., 2012. Recombinant influenza vaccines. Acta Nat. 4 (4), 17−27.

Shams, H., 2005. Recent developments in veterinary vaccinology. Vet. J. 170 (3), 289−299.

Shankar, E.M., Vignesh, R., Ellegård, R., Barathan, M., Chong, Y.K., Bador, M.K., et al., 2014. HIV-*Mycobacterium tuberculosis* co-infection: a 'danger-couple model' of disease pathogenesis. Pathol. Dis. 70 (2), 110−118. Available from: https://doi.org/10.1111/2049-632X.12108.

Shi, X., Lu, W., Wang, Z., Pan, L., Cui, G., Xu, J., et al., 2014. Programmable DNA tile self-assembly using a hierarchical sub-tile strategy. Nanotechnology 25, 075602.

Silveira, M.M., Oliveira, T.L., Schuch, R.A., McBride, A.J.A., Dellagostin, O.A., Hartwig, D.D., 2017. DNA vaccines against leptospirosis: a literature review. Vaccine 35 (42), 5559−5567.

Singh, R.P., Saravanan, P., Sreenivasa, B.P., Singh, R.K., Bandyopadhyay, S.K., 2004. Prevalence and distribution of peste des petits ruminants virus infection in small ruminants in India. Rev. Sci. Tech. (Int. Off. Epizoot.) 23 (3), 807−819.

Singh, R., Singh, K.P., Cherian, S., Saminathan, M., Kapoor, S., Reddy, G.B.M., et al., 2017. Rabies—epidemiology, pathogenesis, public health concerns and advances in diagnosis and control: a comprehensive review. Vet. Q. 37 (1), 212−251. Available from: https://doi.org/10.1080/01652176.2017.1343516.

Sivakumar, T., Hayashida, K., Sugimoto, C., Yokoyama, N., 2014. Evolution and genetic diversity of *Theileria*. Infect. Genet. Evol. 27, 250−263.

Smith, D.R., 2014. Vaccination of cattle against *Escherichia coli* O157:H7. Microbiol. Spectr. 2 (6). Available from: https://doi.org/10.1128/microbiolspec.EHEC-0006-2013.

Stein, R.A., Katz, D.E., 2017. *Escherichia coli*, cattle and the propagation of disease. FEMS Microbiol. Lett. 364. Available from: https://doi.org/10.1093/femsle/fnx050.

Swayne, D.E., 2012. Impact of vaccines and vaccination on global control of avian influenza. Avian Dis. 56 (4 Suppl), 818−828.

Takamura, K., Okada, N., Ui, S., Hirahara, T., Shimizu, Y., 2000. Protection studies on winter dysentery caused by bovine coronavirus in cattle using antigensprepared from infected cell lysates. Can. J. Vet. Res. 64 (2), 138−140.

Takamura, K., Matsumoto, Y., Shimizu, Y., 2002. Field study of bovine coronavirus vaccine enriched with hemagglutinating antigen for winterdysentery in dairy cows. Can. J. Vet. Res. 66 (4), 278−281.

Tewari, A.K., Maharana, B.R., 2011. Control of poultry coccidiosis: changing trends. J. Parasit. Dis. 35 (1), 10−17.

Thomas, C., Young, N.J., Heaney, J., Collins, M.E., Brownlie, J., 2013. Evaluation of efficacy of mammalian and baculovirus expressed E2 subunit vaccine candidates to bovine viral diarrhoea virus. Vet. Microbiol. 162 (2-4), 437−446.

Uzal, F.A., 2012. Evidence-based medicine concerning efficacy of vaccination against *Clostridium chauvoei* infection in cattle. Vet. Clin. N. Am. Food Anim. Pract. 28, 71−77.

van Engelenburg, F.A., Kaashoek, M.J., Rijsewijk, F.A., van den Burg, L., Moerman, A., Gielkens, A.L., et al., 1994. A glycoprotein E deletion mutant of bovine herpesvirus 1 is avirulent in calves. J. Gen. Virol. 75 (Pt 9), 2311−2318.

van Gelder, P., Makoschey, B., 2012. Production of viral vaccines for veterinary use. Berl. Münch. Tierärzt. Wochenschr. 125 (3−4), 103−109. Available from: https://doi.org/ 10.2376/0005-9366-125-103.

Vandersmissen, A., Welburn, S., 2014. Current initiatives in One Health: consolidating the One Heatlh Global Network. Sci. Tech. Rev. 33 (2), 421−432.

Verma, R., Jaiswal, T.N., 1998. Haemorrhagic septicaemia vaccines. Vaccine 16 (11-12), 1184−1192.

Webster, R.G., Bean, W.J., Gorman, O.T., Chambers, T.M., Kawaoka, Y., 1992. Evolution and ecology of influenza A viruses. Microbiol. Rev. 56 (1), 152−179.

Wua, J., Wub, Y., Shienb, J., Hsuc, Y., Chend, C., Shiehb, H., et al., 2011. Recombinant proteins containing the hypervariable region of the haemagglutinin protect chickens against challenge with *Avibacterium paragallinarum*. Vaccine 29, 660−667.

Xiang, Z.Q., Gao, G.P., Reyes-Sandoval, A., Li, Y., Wilson, J.M., Ertl, H.C., 2003. Oral vaccination of mice with adenoviral vectors is not impaired by preexisting immunity to the vaccine carrier. J. Virol. 77, 10780−10789.

Yang, D.K., Kim, H.H., Lee, K.W., Song, J.Y., 2013. The present and future of rabies vaccine in animals. Clin. Exp. Vaccine Res. 2, 19−25.

Yoo, S.J., Kwon, T., Lyoo, Y.S., 2018. Challenges of influenza A viruses in humans and animals and current animal vaccines as an effective control measure. Clin. Exp. Vaccine Res. 7 (1), 1−15.

Yuan, Y., Zhang, Z.P., He, Y.N., Fan, W.S., Dong, Z.H., Zhang, L.H., et al., 2018. Protection against virulent infectious bronchitis virus challenge conferred by a recombinant baculovirus co-expressing S1 and N proteins. Virus 10 (7), E347. Available from: https://doi.org/10.3390/v10070347.

Yun, S.I., Lee, Y.M., 2014. Japanese encephalitis: the virus and vaccines. Human Vaccines and Immunotherapeutics 10 (2), 263−279. Available from: https://doi.org/10.4161/ hv.26902. Epub 2013.

Zhang, N., Huang, D., Wu, W., Liu, J., Liang, F., Zhou, B., et al., 2018. Animal brucellosis control or eradication programs worldwide: a systematic review of experiences and lessons learned. Prev. Vet. Med. Available from: https://doi.org/10.1016/j. prevetmed.2018.10.002.

Further reading

Chen, H., Cui, P., Cui, B., Li, H., Jiao, X., Zheng, L., et al., 2011. Immune responses of chickens inoculated with a recombinant fowlpox vaccine coexpressing glycoprotein B of infectious laryngotracheitis virus and chicken IL-18. FEMS Immunol. Med. Microbiol. 63, 289−295.

Dellagostin, O.A., Grassmann, A.A., Rizzi, C., Schuch, R.A., Jorge, S., Oliveira, T.L., et al., 2017. Reverse vaccinology: an approach for identifying leptospiral vaccine candidates. Int. J. Mol. Sci. 18, 158−174.

Desin, T.S., Köster, W., Potter, A.A., 2013. Salmonella vaccines in poultry: past, present and future. Expert Rev. Vaccines 12 (1), 87−96.

Dhama, K., Chauhan, R.S., Mahendran, M., Malik, S.V.S., 2009. Rotavirus diarrhea in bovines and other domestic animals. Vet. Res. Commun. 33, 1−23.

Diego, E., Gomez, J., Weese, S., 2017. Viral enteritis in calves. Can. Vet. J. 58, 1267−1274.

Dimitrova, K.M., Afonsoa, C.L., Yub, Q., Millera, P.J., 2017. Newcastle disease vaccines—a solved problem or a continuous challenge. Vet. Microbiol. 206, 126−136. Available from: https://doi.org/10.3390/ijms18010158.

Gómez, L., Alvarez, F., Betancur, D., Oñate, A., 2018. Brucellosis vaccines based on the open reading frames from genomic island 3 of *Brucella abortus*. Vaccine 36, 2928−2936.

Idrees, M.A., Younus, M., Farooqi, S.H., Khan, A.U., 2018. Blackleg in cattle: current understanding and future research perspectives—a review. Microb. Pathog. 120, 176−180. Available from: https://doi.org/10.1016/j.micpath.2018.04.047.

James, A.R., 2011. Veterinary vaccines and their importance to animal health and public health. Procedia Vaccinol. 5, 127−136.

Karayela, I., Fehérb, E.Å., Martonb, S., Coskunc, N., Bányaib, K., Alkana, F., 2017. Putative vaccine breakthrough event associated with heterotypic rotavirus infection in newborn calves, Turkey. Vet. Microbiol. 201, 7−13.

Kiril, M., Dimitrova, C.L., Afonsoa, Q.Y., Patti, J., 2017. Miller Newcastle disease vaccines—a solved problem or a continuous challenge. Vet. Microbiol. 206, 126−136.

Kirkwood, C.D., Ma, L., Carey, M.E., Steele, A.D., 2017. The rotavirus vaccine development pipeline. Vaccine S0264-410X (17), 30410−30413.

Lee, N., Lee, J., Park, S., Song, C., Choi, I., Lee, J., 2012. A review of vaccine development and research for industry animals in Korea. Clin. Exp. Vaccine Res. 1, 18−34.

Lubroth, J., Rweyemamu, M.M., Viljoen, G., Diallo, A., Dungu, B., Amanfu, W., 2007. Veterinary vaccines and their use in developing countries. Rev. Sci. Tech. (Int. Off. Epizoot.) 26 (1), 179−201.

Morales-Erasto, V., Maruri-Esteban, E., Trujillo-Ruíz, H.H., Talavera-Rojas, M., Blackall, P.J., Soriano-Vargas, E., 2014. Protection conferred by infectious coryza vaccines against emergent *Avibacterium paragallinarum* Serovar C-1. Avian Dis. 59 (1), 162−164.

Na, W., Yeom, M., Yuk, H., Moon, H., Kang, B., Song, D., 2016. Influenza virus vaccine for neglected hosts: horses and dogs. Clin. Exp. Vaccine Res. 5, 117−124.

Nascimento, I.P., Leite, L.C.C., 2012. Recombinant vaccines and the development of new vaccine strategies. Braz. J. Med. Biol. Res. 45 (12), 1102−1111.

Natalie, A.P., Bryce, M.B., 2015. Immunity and vaccination against tuberculosis in cattle. Curr. Clin. Microbiol. Rep. 2, 44−53.

Nettleton, P., Russell, G., 2017. Update on infectious bovine rhinotracheitis. In Practice 39, 255−272.

Paillot, R., 2014. A systematic review of recent advances in equine influenza vaccination. Vaccines 2, 797−831.

Pourasgari, F., Kaplon, J., Karimi-Naghlani, S., Fremy, C., Otarod, V., Ambert-Balay, K., et al., 2016. The molecular epidemiology of bovine rotaviruses circulating in Iran: a two-year study. Arch. Virol. 161 (12), 3483−3494.

Rajendran, P., Kang, G., 2014. Molecular epidemiology of rotavirus in children and animals and characterization of an unusual G10P[15] strain associated with bovine diarrhea in south India. Vaccine 32S, A89−A94.

Rao, T.S., Arora, R., Khera, A., Tate, J.E., Parashar, U., Kang, G., 2014. Insights from global data for use of rotavirus vaccines in India. Vaccine 32 (Suppl 1), A171−A178.

Redding, L., Weiner, D.B., 2009. DNA vaccines in veterinary use. Expert Rev. Vaccines 8 (9), 1251−1276.

Sandbulte, M.R., Spickler, A.R., Zaabel, P.K., Roth, J.A., 2015. Optimal use of vaccines for control of influenza A virus in swine. Vaccines 3, 22−73.

Shahid, N., Rao, A.Q., Kristen, P.E., Ali, M.A., Tabassum, B., Umar, S., et al., 2017. A concise review of poultry vaccination and future implementation of plant-based vaccines. World's Poult. Sci. J. 73, 1−12.

Tate, J.E., Arora, R., Bhan, M.K., Yewale, V., Parashar, U.D., Kang, G., 2014. Rotavirus disease and vaccines in India: a tremendous public health opportunity. Vaccine 32S, 7−12.

Umthong, S., Buaklin, A., Jacquet, A., Sangjun, N., Kerdkaew, R., Patarakul, K., et al., 2015. Immunogenicity of a DNA and recombinant protein vaccine combining LipL32 and Loa22 for leptospirosis using chitosan as a delivery system. J. Microbiol. Biotechnol. 25 (4), 526−536.

Wahren, B., Margaret, A.L., 2014.). DNA vaccines: recent developments and the future. Vaccines 2, 785−796.

Wray, C., 1994. Mamalian salmonellosis. In: Beran, G.W. (Ed.), Hand Book of Zoonosis, second ed. CRC Press, New York, pp. 291−300.

Zamri-Saad, M., Kamarudin, M.I., 2016. Control of animal brucellosis: the Malaysian experience. Asian Pac. J. Trop. Med. 9 (12), 1136−1140.