CHAPTER 1

Vaccination – Facts and Importance

1.1 Introduction

India is the world’s largest producer of milk. In 2003-04 India produced 850 million tons of milk. India tops in cattle wealth in the world. 15% of the world’s cattle and 57% of buffaloes are in India. The total number of the cattle in India as per the census of 2003 is 185 million and 98 million buffaloes. In Tamilnadu, as per the 126th livestock and poultry census 2000, the total cattle population is 93.63 lakh, which accounts for 35.8% of the total livestock population in the country (1). Cattle are raised as dairy animal for milk and other dairy products, as livestock for meat (beef), and as draft animals (pulling carts, plough). Other products include leather and dung for manure or fuel. So cattle should be protected from bacterial and viral diseases to increase the economic status of a country. In egg production India ranks fifth in the world. In livestock and poultry farm, animals should be vaccinated to protect from diseases.

Vaccination is the administration of antigenic material (the vaccine) to produce immunity to a disease. It is considered to be the most effective and cost-effective method of preventing infectious disease. A vaccine is a biological preparation which is used to establish or improve immunity to a particular disease. Vaccines may be monovalent (also called univalent) or
multivalent (also called polyvalent). A monovalent vaccine is designed to immunize against a single antigen or single microorganism (2). A multivalent or polyvalent vaccine is designed to immunize against two or more strains of the same microorganism (3). In certain cases a monovalent vaccine may be preferable for rapidly developing a strong immune response (4). The material administered can either be live but weakened forms of pathogens such as bacteria or viruses killed or inactivated forms of these pathogens or purified material such as proteins.

1.2 History of vaccination

The tradition of vaccination may have originated in India in AD 1000 (5). The mention of vaccination in the Sact'eya Grantham, an Ayurvedic text, was noted by the French scholar Henry Marie Husson in the journal Dictionnaire des sciences mé'dicales (6). Almroth Wright, the professor of pathology at Netley, further helped shape the future of vaccination by conducting limited experiments on the professional staff at Netley, including himself. The outcome of these experiments resulted in further development of vaccination in Europe (7).

Smallpox was the first disease people tried to prevent by purposely inoculating themselves with other types of infections; smallpox inoculation was started in China or India before 200 BC (8). In 1718, Lady Montague a famous English letter writer and wife of the English ambassador reported that
Turks have a habit of deliberately inoculating themselves with fluid taken from mild cases of smallpox and she inoculated her own children (9). Scientific description of vaccination operation was submitted to the Royal Society in 1724 by Dr.Emmanuel Timoni, who had been the Montagu’s family physician in Istanbul.

The word vaccination was first used by Edward Jenner an English physician. Louis Pasteur further adapted this in his pioneering work in microbiology. In Latin, ‘vacca’ means cow. Vaccination is so named because the first vaccine was derived from cow pox virus, a virus affecting cows, which provides a degree of immunity to smallpox. In common speech, vaccination and immunization generally have the same meaning. This distinguishes it from inoculation which uses unweakened live pathogens, although in common usage either is used to refer to an immunization. The word ‘vaccination’ was originally used specifically to describe the injection of smallpox vaccine (10).

**Vaccine targets**

Vaccines for bacterial pathogens of livestock and poultry have historically been targeted at organisms that were significant disease threats in the target species. In the case of zoonotic diseases, these included brucellosis, anthrax, clostridial disease and others. Vaccination was able to protect not only the immunized host, but it also reduced the risk of transmission to humans through a reduction in the pathogen reservoir.
1.3 Types of vaccines

All vaccinations work by presenting a foreign antigen to the immune system in order to evoke an immune response, but there are several ways to do this. The three types are

(i) An inactivated vaccine consists of virus particles which are grown in culture and then killed using a method such as heat or a chemical like formaldehyde. The virus particles are destroyed and cannot replicate, but the virus capsid proteins are intact enough to be recognized by the immune system and evoke an immune response. When manufactured correctly, the vaccine is not infectious, but improper inactivation can result in intact and infectious particles. Since the properly produced vaccine does not reproduce, booster shots are required periodically to reinforce the immune response.

(ii) In an attenuated vaccine, live virus particles with very low virulence are administered. They will reproduce, but very slowly. Since they reproduce and continue to present antigen beyond the initial vaccination, boosters are required less often.

(iii) A subunit vaccine presents an antigen to the immune system without introducing viral particles, whole or otherwise. One method of production involves isolation of a specific protein from a virus and administering this by itself. A weakness of this technique is that
isolated proteins can be denatured and will then bind to different antibodies than the proteins in the virus. A second method of subunit vaccine is the recombinant vaccine, which involves introducing a protein gene from the targeted virus into a suitable vector viz. prokaryotic, Eukaryotic or another virus.

Live Vaccines

Live vaccines are also termed as live virus, live attenuated and avirulent vaccines. A live vaccine is a vaccine containing whole, live viruses (and/or bacteria). These viruses are non-dangerous strains of virus which are very closely related to the wild-type, disease-causing viruses used to protect animal. These viruses have many of the exact same antigens (proteins/sugars that the immune system must recognize as foreign to trigger an attack) present on their surface that the disease causing organisms do and as a result, the antibodies and memory T and B cells created following the vaccination will be able to protect the animal against the dangerous viral (and bacterial) organisms that bear those same surface antigens. When these vaccine viruses are injected into the animal, they multiply within the cells and tissues of the animal, growing to large proportions. It sounds terrible, but it is actually a good thing that they do multiply: greater numbers of viral particles mean that the immune system will be exposed to greater volumes of viral vaccine antigens. A greater immune response will be triggered to 'kill' off these
millions of viral antigens and the end result will be higher levels of protective antibodies floating through the blood and greater numbers of memory T and B cells waiting to protect the body in the face of attack with a real, disease causing organism. It is because of this greater immune protective response to the live vaccines, that live attenuated vaccines are preferred over killed-type vaccines for immunizing normal animals where possible.

*Live vaccines – potential problems*

- Because the virus is alive, it has to be stored carefully or the virus can die and become ineffective.

- Potential to cause disease in pregnant animals.

- Certain live vaccines can cause severe complications: e.g. live rabies vaccines can cause fatal neurological disease in some dogs and cats.

- Vaccines that have not been produced properly and undergone adequate quality control may contain virulent organisms which could produce severe disease (this is very rare).

- Some live vaccines, if given by the wrong route, can cause severe illness (e.g. injectable cat flu vaccine viruses that accidentally get inhaled by a cat will produce marked signs of cat-flu and intranasal Bordetella vaccine viruses that get injected can cause liver damage and death of the animal).
• Live vaccines tend to 'take up the time' of a lot of the body's white blood cells, leaving fewer white blood cells available to fight other infections. This relative immunosuppressant may leave the body less defended and thus more vulnerable to other diseases during the period of time that the vaccine is present. This is less of a problem with killed vaccines.

• A lack of preservatives in these vaccines means that their shelf life might be shorter.

*Advantages of Live attenuated bacterial vaccines*

Live attenuated bacterial vaccines have several potential advantages over killed or subunit products, but their use in veterinary medicine has been limited to date. These advantages include the presence of the full repertoire of protective antigens, including those produced in vivo, the ability to induce balanced Th1/Th2 responses, the potential for single dose administration and lower production costs than subunit vaccines. Historically, attenuation has been carried out by using altered growth conditions, chemical mutagenesis or passage through alternative hosts. The use of Brucella abortis strain 19 is an excellent example of a traditional live vaccine that has proved effective in the control of brucellosis (11). There are two areas that have limited the use of live vaccines in animals. First, the routine use of antibiotics in animal husbandry has precluded their use for obvious reasons, since there is a need for limited replication and transient colonization to occur. The second issue
has been one of safety; since the attenuating mutation(s) were not known in many prototype vaccines, there have been concerns of reversion to virulence. Advances in molecular genetics in the 1970s and 1980s made it possible to rapidly construct defined insertions and deletions in specific genes, making rational attenuation possible and the first live attenuated bacterial vectors included transposon insertions of Salmonella enterica serovars (12). These defined mutations resulted in safer vaccine strains, which could also be used for delivering a variety of foreign antigens to animals (13, 14). Furthermore, by selecting the appropriate target genes for deletion, it is possible to tailor the degree of attenuation in a similar fashion to that routinely carried out in the development of modified live viral vaccines.

*Killed vaccines - potential problems*

1. Poorer, shorter-duration cell-mediated and humoral immunity (unless lots of virus particles and/or adjuvants are included).

2. Greater risk of causing allergic reactions and injection site reactions because of the presence of large volumes of virus material and/or adjuvants.

3. Some products are not safe for use in pregnant animals.

4. Most require a minimum of two doses to achieve the desired effect (risk of vaccine reaction with the second dose).

5. They are generally more expensive to produce.

6. Must be given by injection (not available in other routes of administration - intranasal etc.)
Benefits of Killed vaccines

1. Unlikely to cause disease in immunocompromised or pregnant or newborn animals (though the response to vaccination in immunosuppressed individuals might be low).

2. Do not tend to cause the same relative immunosuppressant and vulnerability to other diseases that the live vaccines do.

3. They store for longer periods.

1.4 Adjuvant and preservatives

Adjuvant was originally described by Ramon (15) as ‘helper’ substances that can enhance the immune responses to the antigen alone. Adjuvant has been developed mainly by trial and error, screening a wide variety of natural and synthetic molecules. Inactivated vaccines typically contain one or more adjuvant, used to boost the immune response. Tetanus Toxoid, for instance, is usually adsorbed on to alum. This presents the antigen in such a way as to produce a greater action than the simple aqueous tetanus toxoid. People who get an excessive reaction to adsorbed tetanus toxoid may be given the simple vaccine when time for a booster occurs. In the preparation for the 1990 Gulf campaign, Pertussis vaccine (not cellular) was used as an adjuvant for Anthrax vaccine. This produces a more rapid immune response than giving only the Anthrax, which is of some benefit if exposure might be imminent. They may also contain preservatives which are used to prevent contamination with bacteria and fungi. Several preservatives are available, including thiomersal, 2-phenoxyethanol and formaldehyde.
Innovative vaccines

A number of innovative vaccines are also in development and in use:

(i) Conjugate – certain bacteria have polysaccharide outer coats that are poorly immunogenic. By linking these outer coats to proteins (e.g. toxins) the immune system can be led to recognize the polysaccharide as if they were a protein antigen. This approach is used in the Haemophilus influenzae type B vaccine.

(ii) Recombinant vector-by combining the physiology of one microorganism and the DNA of the other, immunity can be created against diseases that have complex infection process.

(iii) DNA vaccine – in recent years a new type of vaccine, created from an infectious agent’s DNA called DNA vaccine, has been developed. It works by insertion into human or animal cells, of viral or bacterial DNA. Some cells of the immune system (memory cells) that recognize the proteins expressed will mount an attack against these proteins and cells expressing them. Because these cells live for a very long time, if the pathogen that normally expressed these proteins is encountered at a later time, they will be attacked instantly by the immune system (anamnestic response).

(iv) Synthetic vaccines - are composed mainly or wholly of synthetic peptides, carbohydrates or antigens. Vaccines may be monovalent or multivalent. A monovalent vaccine is designed to immunize against a
single antigen or single microorganism. A multivalent vaccine is
designed to immunize against two or more strains of the same
microorganism, or it can be a combined vaccine against two or more
microorganisms (e.g. DTP, MMR). Most of the literature dealing with
DNA vaccines has described the use of viral antigens delivered in
mouse models and the results have been promising. However, when
large animals have been used, results have been disappointing. Cox et
al (16) described the first example of vaccination of a non-rodent
species with a DNA vaccine and they showed that immunization of
cattle with nucleic acid encoding a bovine herpesvirus-1 glycoprotein
was able to induce cellular and humoral immune responses. However,
the dose of plasmid DNA was high, and repeated immunizations were
required for the induction of immunity. Since that time, DNA vaccines
have been shown to be effective in cattle, sheep, poultry, horses and
fish and commercially available products have been produced for the
latter two species. No vaccines for bacterial diseases are currently
available, although experimental vaccines have been described for
Mycobacterium avium subspecies paratuberculosis, Campylobacter
jejuni, B. anthracis, Pasteurella multocida, Salmonella species and
others. These are unlikely to see commercial development until the
plasmid dose can be reduced and the method of delivery optimized
(e.g. prime-boost strategies). Gerdts et al (17) demonstrated that in
utero immunization of sheep resulted in protective immunity, a finding
which has implications for potential fetal delivery of animal vaccines.
Live vectors

Live vectored vaccines facilitate the delivery of recombinant proteins expressed within the vector itself, or genetic information either integrated into the genome or as plasmid DNA. Both viral and bacterial vectors have been developed for vaccine delivery in animal that are incapable of reverting to full virulence and are therefore safe to use. Various bacterial delivery systems have been optimized for the delivery of recombinant antigens as well as plasmid DNA. For example, S. enterica serovars or Shigella species can target mucosal tissues and deliver the foreign antigen specifically to antigen-presenting cells (APCs) via bacterial secretion systems (18 to 20). Other vectors include Staphylococcus, microorganisms such as Salmonella, Shigella, BCG, Corynebacterium, Bacillus, Yersinia, Vibrio, Erysipelothrix and Bordetella species (21 to 26). Other bacterial vectors have been demonstrated to carry plasmid DNA across the mucosal surfaces (27 to 29) and more recently, bacterial ghosts were demonstrated to represent effective means to deliver plasmid DNA (30). Several viral vectors including poxviruses, herpesviruses and adenoviruses have been used as vectors for veterinary vaccines (31). The usefulness of viral vectors for livestock species and poultry greatly depends on their host range and tropism. Ideally, a vector has a broad host range, infects and replicates within a wide range of tissues and ensures optimal posttranslational modifications of the recombinant antigen including proper folding and processing (32). Canary pox-based
vaccines are already licensed for the use in both large and small animals, and other viral vectors are currently being evaluated for vaccine delivery including DNA viruses such as adenoviruses, herpes viruses and RNA viruses such as Newcastle disease virus (NDV), Venezuelan equine encephalitis (VEE), Semliki forest virus (SFV) and a few retroviruses. For example, a recombinant alphaherpesvirus, pseudorabies virus (PRV), carrying the E1 glycoprotein of the classical swine fever virus (CSFV), was used by van Zijl et al to protect pigs against challenge infection with CSFV (33). Kit et al used the bovine herpesvirus type 1 (BHV-1) to deliver the viral protein (VP) 1 of foot-and-mouth disease virus (FMDV) to young calves,(34) and Kweon et al used BHV-1 as a vector for delivering the glycoprotein E2 of the bovine virus diarrhea virus (BVDV) to calves (35). All the above and numerous other examples demonstrate the potency of live viral vectors for vaccine delivery.

1.5 Methods of administration

A vaccine administration may be oral, by injection (intramuscular, intradermal, and subcutaneous), by puncture, transdermal or intranasal (36).

1.6 Immunity

The immune system recognizes vaccine agent as foreign, destroys them, and ‘remembers’ them. When the virulent version of an agent enters the body, the immune system recognizes the protein coat on the infective agent, and thus is prepared to respond, by (i) neutralizing the target agent before it
can enter cells and (ii) by recognizing and destroying infected cells before that agent can multiply to vast numbers.

**Antigens**

Antigen is any substance that evokes the production of an antibody when introduced into the body. Antigens can enter the body through the respiratory tract, digestive tract, or skin. The most common antigens are proteins such as those found in/on bacteria and viruses.

**Antibodies**

Antibody, is one of a million kinds of normally occurring protein molecules that are produced in the body, is elaborated by cells called lymphocytes and that act primarily as a defense against invasion by foreign substances. An important component of the immune system, antibodies are found in the blood of all vertebrates, in the fraction of the blood called gamma globulin.

The synthesis or manufacture of antibodies is initiated when a foreign substance, referred to as an antigen, enters the body. Lymphocytes respond to the foreign substance by making an antibody with a molecular arrangement that fits the shape of molecules on the surface of the substance so that the antibody combines with it. Common antigens are the protein components of bacteria and viruses. These antigens may enter the body during infection or
may be deliberately introduced by vaccination in order to stimulate the production of antibodies. The binding of antibodies to the surfaces of bacteria, viruses, or toxins can neutralize and eliminate these harmful substances in any or all of three ways: (1) by directly inactivating them, (2) by enabling other blood cells to engulf and destroy them and (3) by weakening their surfaces and rendering them vulnerable to destruction by other blood proteins. Animals do not have antibodies to substances to which they have not been exposed, but one animal is able to produce enough different kinds of antibodies to fit the molecular arrangement of any foreign substance it is likely to encounter as per Burnett’s Clonal hypothesis.

The five known classes of antibody are distinguished by the letters M, G, E, A, and D; all are preceded by the abbreviation Ig for immunoglobulin, another name for antibody. IgM is the first antibody made by newborns and the first made during an infection. IgG is the predominant antibody in serum; it is made on the second exposure to an antigen. IgE is associated with allergy. IgA (secretary Ig) is found in saliva and mother's milk. The role of IgD is not known.

In the 1970s scientists learnt how to fuse these myeloma cells with lymphocytes from tissues that had been exposed to an antigen. The resulting hybrid cells ("hybridomas") were able to produce large amounts of antibody of one specific arrangement ("clones"), called monoclonal antibodies. By selecting the appropriate hybridoma, scientists can obtain pure antibody that
combines with any chosen foreign substance. The use of monoclonal antibodies has become a valuable tool in biology and medicine because pure lines of antibody can combine with and therefore mark, or identify, the component substances of cells and tissues.

The immune system of the young animal contains many different cell types. For the purpose of this discussion, these can be broken up into two main groups:

1) Some cells are non-antigen-specific in their responses. After being called into an area of infection by chemical messages sent out from antigen-specific cells and antigen-specific-antibody-reactions, these cells come into a region of infection in large numbers to do battle. They do battle by either gobbling up any infectious organisms or tissue debris in the area or by releasing nasty chemicals that pretty much blast everything in the local region, including healthy tissue. The non-antigen-specific cells include the pus-forming white blood cells (neutrophils, macrophages) and other inflammatory cells (mast cells, basophils etc). Some of these cells have some ability to identify certain infectious organisms and mount an attack against them, regardless of the presence of an antigen-specific immune response: this ability may allow animals with a very naive immune system (esp. animals that didn't get colostrums) to fight against some infectious organisms to some degree.
2) Some cells are antigen-specific in their responses. Certain lines of cells are designed to only mount a response against certain specific, recognized antigens that are present on the surface of organisms, foreign bodies and other invaders and that are different (foreign) to antigens present on the body’s own cells. Termed T lymphocytes and B lymphocytes large populations of each of these antigen-specific cell types are present in the body at birth. During the period when young animal are in the uterus, every one of these cells is carefully screened by the embryonic immune system, to ensure that they recognize the antigens present on the body’s cell surfaces. The lymphocytes are of most importance when talking about vaccination.

When the animal is first born, although there are lots of lymphocytes (both T cell and B cell varieties) present in the young body, each individual lymphocyte is only able to recognize and bind to a very particular antigen (i.e. just one possible protein or sugar molecule combination among the many millions of foreign antigen combinations present in the environment). Among the many millions of lymphocytes present in the body at birth, the desire is that at least a few among them will have the right combination of surface protein molecules (termed T-cell markers) needed to recognize and bind to any particular antigen that the body might encounter. The significance of this is: when an infectious organism that has not been encountered by the body before attacks, although there will be T lymphocytes and B lymphocytes
present in the body which are capable of recognizing and establishing an immune response against the organism's particular antigens, there will not be that many of them. In the presence of the infectious organisms, the small group of lymphocytes bearing the right antigen-recognition proteins will need to multiply to large numbers before they will be able to mount enough of an immune response (calling in the non-specific inflammatory cells, making enough antibodies etc) to defeat the infection. Thus (particularly in the absence of maternal antibody), the initial immune response to the infection will be weak, allowing the infectious disease to get a head start and make the animal clinically unwell. When the T cells and B cells bearing the right antigen-recognition proteins (T-cell markers) do eventually get to sufficient numbers, they are instrumental in defeating infectious organisms. This is because they have so many mechanisms at their disposal for killing foreign organisms.

*Unvaccinated animals are in risk*

When an animal is born, its immune system has all of the components contained in the immune system of the parent animal; except that it is very *naive* (have never been exposed to any foreign antigens before). Such an animal when exposed to a really virulent strain of infectious disease, its immune system (having never been exposed to the antigens present on the surface of this organism before) will take ages (up to 2 weeks) to mount a
defensive response against the disease. The disease will potentially get a 2 week head-start on the animal without being opposed by its immune system (after all, it takes time for immune cells to divide and build up their forces and start producing protective antibodies). Thus the animal may develop really severe illness and could even die (with distemper, parvovirus and rabies the chance of death is really high).

When exposed to foreign antigens in the presence of chemical messages produced by the T cells, the B lymphocytes bearing the correct antigen-recognition proteins become activated and multiply to large numbers. These activated cells develop into mature B cells termed plasma cells and start making antibodies. Antibodies are proteins that specifically bind to certain foreign antigens (the exact same foreign antigens that the B cell and T cells specifically reacted towards) contained on the surface of infectious or foreign body organisms and cells containing infectious organisms. There are 5 different types of antibodies. These 'complement protein products' produced from enzyme reactions have several roles

a) some travel in the blood as messengers, calling white blood cells into the region to kill the invaders.

b) Some activate these incoming white blood cells (neutrophils, macrophages), inducing them to swallow up the antibody-tagged organism (e.g. bacterium)
c) Some activate inflammatory cells such as mast cells, causing them to release proteins such as histamine and heparin into the region. These products make the local blood vessels dilate (more blood flow to region, bringing in oxygen and nutrients for the inflammatory cells to use) and they make the local blood vessels leaky (this results in more white blood cells and important immune proteins being able to migrate into the region) - resulting in the redness and swelling seen at sites of infection or inflammation.

d) Some of the complement proteins bind to the foreign cell or bacterium, putting holes in the membrane of the invader (thus killing it in a similar way to the cytotoxic T cells).

e) Some of them even make the surfaces of the organism stickier such that they will bind together (termed agglutination) and is unable to move and invade. Overall, the immune system response directly attributed to the B cells and the antibody producing plasma cells is termed **Humoral Immunity**.

When we vaccinate an animal, a small amount of viral or bacterial antigen is injected under the skin of the young animal (which has an inexperiance or naive immune system). This antigen-containing injection can comprise a whole, live, replicating virus (live vaccine) which is not virulent enough to cause disease in the immunologically naive animal, but which has many of the exact same antigens on its surface as the nasty disease-causing
organisms or it can comprise a killed version of the virulent strain of virus (unable to replicate and cause disease), which also contains the surface antigens required to induce the immune system to react.

The immune system attacks the antigens in a similar fashion to that described above and, over 2 weeks, a large population of B cells, T cells and antibodies, which are specific to those injected viral and bacterial surface antigens, forms. Unlike the situation described before, where a virulent strain of organism infected an immunologically naive animal and caused severe disease, the 2-week time period taken to build up the immune system defenses is not an issue here because the organisms injected are either minimally-pathogenic (unable to cause severe disease) or they are killed (unable to replicate). Following this initial exposure to the viral and/or bacterial antigens contained in the vaccine, large numbers of B cells and T cells specific to these antigens will distribute themselves throughout the body's lymphoid tissues, ready to be there to defend against an infectious organism, where ever it may appear. They will then go dormant in these lymphoid tissues, until recognized antigens from an infectious disease-causing organism or a vaccine-organism come along to reactivate them. These B and T cells are termed 'memory cells' because they effectively 'remember' the antigens that the body has fought before. For a period of time, following vaccination, antibodies produced in the response to that first vaccination will also circulate throughout the body, ready to encounter and protect against foreign disease invaders. With some
vaccines, the amount of antibody produced following that initial vaccination will be moderately low and the levels of antibody (mostly IgM antibodies which are the shorter-lived antibody types generally made by plasma cells when they first encounter a new organism) circulating in the body will dwindle away quickly within a few months (not be long-lived). It is when the second (and third) vaccinations are given (1 month and then 2 months later) that the huge populations of 'memory B cells' activate and produce the massive levels of longer-lasting antibodies (IgG type) required to achieve year-long humoral protection. This is the main reason that animals getting vaccinated for the first time generally receive a 'course' of two or three vaccinations 2-4 weeks apart, it is to build up their levels of antibodies against the foreign pathogens such that these antibody levels will provide them with protection for at least a year to 3-years. It is also important to test antibody levels for determining whether an animal requires re vaccination.

1.7 Efficacy

Vaccines do not guarantee complete protection from a disease. Sometimes this is because the host's immune system simply doesn't respond adequately or at all. This may be due to a lowered immunity in general or because the host's immune system does not have a B-cell capable of generating antibodies to that antigen. Adjuvant is typically used to boost immune response. Adjuvant is sometimes called the 'dirty little secret of vaccines' in the scientific community, as not much is known about how
adjuvant works. Most often aluminum adjuvants are used, but adjuvant like squalene are also used in some vaccines and more vaccines with squalene and phosphate adjuvant are being tested.

The efficacy or performance of the vaccine depends on number of factors. The disease itself, the strain of vaccine, whether one kept to the timetable for the vaccinations, some individuals are ‘non-responders’ to certain vaccines, meaning that they do not generate antibodies even after being vaccinated correctly and other factors such as ethnicity or genetic predisposition.

1.8 Vaccination of animal

Animals are vaccinated both to prevent their contracting disease and transmission of disease to human (37). Both animals kept as pets and animal rose for production traits are vaccinated. In some instances, wild animal may also be vaccinated. This is sometimes accomplished with vaccine-laced food (bite-vaccine) spread in a disease-prone area and has been used to attempt to control rabies.
References


2 *Monovalent* at Dorland's Medical Dictionary.

3 Polyvalent vaccine at *Dorlands Medical Dictionary*.

4 Questions and answers on monovalent oral polio vaccine type 1 (moPV1) “Issued jointly by WHO and UNICEF”


