WORLD SMALL ANIMAL VETERINARY ASSOCIATION

VACCINATION GUIDELINES FOR THE OWNERS AND BREEDERS OF DOGS AND CATS

WSAVA Vaccination Guidelines Group

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INTRODUCTION

Vaccination of dogs and cats protects them from infections that may be lethal or cause serious disease. Vaccination is a safe and efficacious practice that in many countries has had major impact on improving the quality of life of small companion animals. The success of small animal vaccination programmes over the past five decades mirrors the success of vaccination in controlling disease in the human population.

Owners and breeders of dogs and cats will be very aware of the prominent media exposure that has been given to the practice of vaccination in human and animal populations in the past two decades. This public attention has focussed on the rare instances of adverse events that might follow administration of vaccines to people or animals. The medical and veterinary professions have devoted considerable time and effort to addressing vaccination issues and developing protocols for the administration of these products that increase safety and minimize the already low risks associated with vaccination. Many owners and breeders will be aware of the expert groups that have been convened to offer medical and veterinary practitioners guidance on the optimum methods of delivering vaccination to their patients. In veterinary medicine, one such body is the World Small Animal Veterinary Association (WSAVA) Vaccination Guidelines Group (VGG) that has provided science-based advice to small animal practitioners in a document originally published in 2007 and updated in 2010.

The VGG, is however, very aware that high quality scientific information related to the practice of small animal vaccination is not readily accessed by the lay public in a form that is comprehensible. Unfortunately, there is much misinformation that is

readily promulgated via the internet by individuals and groups that lack scientific credibility. This has led to public concern and to the misguided practice of refusing vaccines when offered by the veterinarian. Failure to appropriately vaccinate your dog or cat makes them susceptible to lethal infectious diseases and the benefit of vaccination far outweighs any risk of an adverse event following vaccination.

In order to address these public concerns, the VGG has prepared the following document. This provides, for the first time, a concise summary of this area in lay terms that should be readily understood by pet owners and breeders. The information provided is based on current scientific knowledge and is prepared by internationally recognized experts in small animal microbiology, immunology and vaccinology. The document initially gives an account of the major vaccine-preventable infectious diseases of small companion animals and then discusses the fundamentals of the immune response and the immunological principles of vaccination. We address the public debate over vaccination that has led to the development of vaccination guidelines and explain the guidelines to which we have encouraged the veterinary profession to adhere. Finally, we also discuss adverse events and what you should do if you suspect that a vaccine administered to your pet might be responsible for such an effect. We realize that scientific terminology can sometimes appear impenetrable and so have provided a glossary of terms to aid in your understanding. A major component of the written document is a set of images that present to you in graphic visual form the consequences of failing to protect your pet through vaccination. These infectious diseases have not disappeared and even in developed nations with good vaccination programmes there continue to be localized outbreaks of infection and disease. We encourage

you to study this document and carefully consider the content in order to maximize the well-being of our small companion animals.

MAJOR INFECTIOUS DISEASES OF THE DOG AND CAT

Canine Distemper

This canine virus disease is seen regularly in developing countries, where vaccination of dogs is not commonplace, and in western countries when negligence or philosophical/religious reasons have left animals unvaccinated and unprotected. Through the use of **live attenuated vaccines**, canine distemper has been generally well controlled worldwide, but cases are repeatedly reported from European countries, the USA and Japan. Eradication of canine distemper is not possible, because the virus occurs in **wild animals** (e.g. badgers, foxes, martins, ferrets, mongoose, raccoons, mink, seals, skunks and others) and from there can re-enter domestic dog populations.

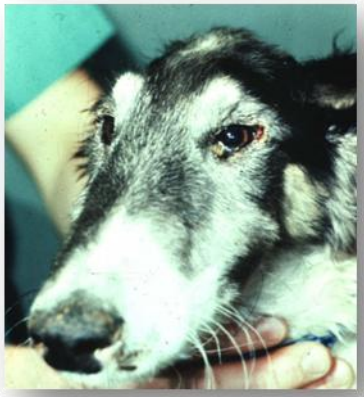
The canine distemper virus (CDV) is a relative of the **human measles** and bovine rinderpest viruses, and it is possible (and has been practiced in the past) to protect dogs against canine distemper using a measles vaccine. CDV occurs as a **single serotype**, but genetic variants have been shown in the laboratory and new strains have occurred in the field that have infected large cats (e.g. lions), seals and sea lions. These new strains also infect different tissues of the animal compared with the original strain of CDV. Importantly, incubation periods for the virus have changed so that one may see little or no disease for up to 6 weeks after infection, after which the animal may develop the classical clinical signs of infection. Claims of

virulent variants against which the current vaccines would not protect have never been substantiated. The virus is **fragile** and common **detergent-containing disinfectants rapidly destroy its infectivity**.

Canine distemper is a disease of young animals and **puppies 3 – 6 months of age** are particularly **susceptible**. The virus spreads through **aerosol droplets** produced during coughing and through contact with nasal and ocular secretions, faeces and urine. **Incubation periods** range from 2 – 6 weeks and a first bout of fever is seen 3 – 6 days after infection. After inhalation, the virus initially **replicates** in the **lymphoid tissue** of the respiratory tract, then enters the blood stream (producing a **viraemia**) and subsequently multiplies in other lymphoid and epithelial tissues. Its preference for lymphoid, epithelial and nervous tissues leads to disease signs in the respiratory, gastrointestinal and central nervous systems. As a consequence of **lymphoid depletion**, **immunosuppression** arises, which allows **secondary infections** to occur. Typical pathological features include interstitial **pneumonia** and **encephalitis** with **demyelination**. Hyperkeratosis of the foot pads ('**hard pad disease**') was very common with the original acute biotype of the virus, but the subacute biotypes that commonly infect dogs today are less likely to cause hard pad disease.

The highest mortality rates (often over 50%) are observed in puppies, mostly as a consequence of complications such as anorexia, pneumonia and encephalitis. In older susceptible (non-immune) dogs CDV infection may cause respiratory disease that is indistinguishable from 'kennel cough' and some dogs may develop **encephalomyelitis** (neurological) or **vestibular disease**. Older non-immune dogs can and do develop severe disease and die from distemper.

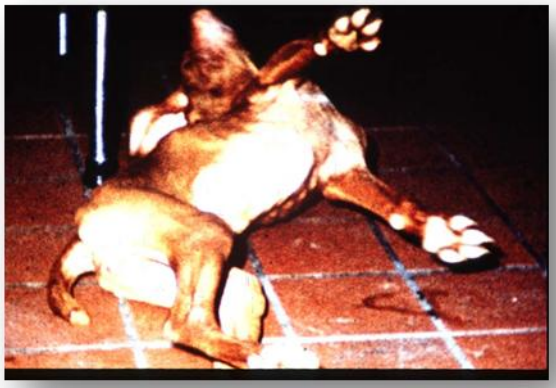
Common disease signs are a runny nose, vomiting and diarrhoea, dehydration, excessive salivation, coughing, laboured breathing, crusty discharge from the eyes, loss of appetite and weight loss.



Discharge from the eyes and nose in a dog with distemper (Photograph courtesy LE Carmichael, MJ Appel).

Central nervous signs include localized muscle twitching, seizures with salivation, and jaw movements commonly described as ‘chewing gum fits’. This **distemper myoclonus** may progress and worsen, advance to convulsions and be followed by death. Once the systemic disease develops it may last for only 10 days. Neurological damage may be due directly to the virus (acute) or to the immune response to the virus. The clinical signs of neurological disease may not appear until several weeks (acute encephalitis), months (subacute encephalitis) or even years later (‘old dog encephalitis’). Survivors usually continue to show twitching (‘tics’) of varying severity and duration.

Neurological signs ('head pressing') in a dog with distemper (Photograph courtesy LE Carmichael, MJ Appel).

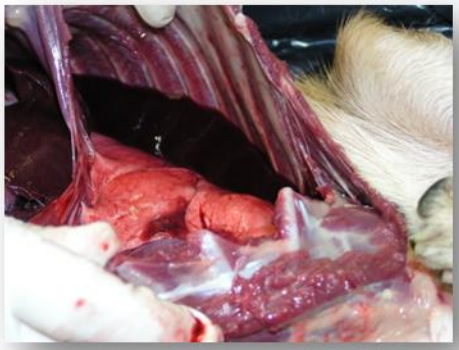


Neurological signs (seizuring) in a dog with distemper (Photograph courtesy LE Carmichael, MJ Appel).

Infectious Canine Hepatitis (ICH)

Infectious canine hepatitis is caused by **canine adenovirus type 1** (CAV-1). The disease has been recognized rarely in the last decades in those countries with effective vaccination programmes. However, the causative agent is still prevalent in developing countries where only a small percentage of dogs is vaccinated and in feral carnivore populations worldwide. Therefore vaccination must be continued in order to prevent outbreaks of this devastating disease. The same virus has caused **encephalitis** in **foxes and other wild canid species**.

Dogs < 1 year of age are most often affected. This environmentally **resistant virus** is spread by **direct and indirect contact** and enters the body by **inhalation and ingestion**. It **replicates** first in the **tonsils**, is then distributed through the blood stream, with secondary infection and **replication in the liver and kidneys**. Mortality rates reach 50% in young dogs.

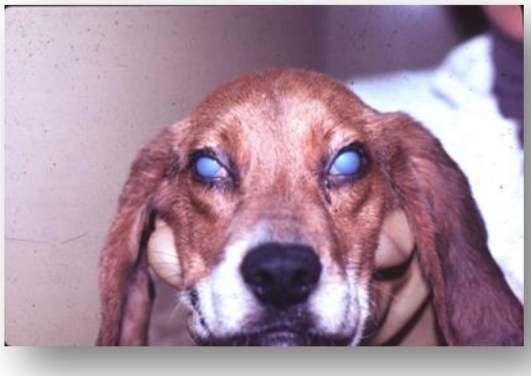


Bleeding into the chest cavity in a dog with CAV-1 infection (Photograph courtesy RD Schultz, LJ Larson)

Clinical signs include depression, fever, vomiting, diarrhoea and discharges from the nose and eyes.

Puppy with CAV-1 infection showing jaundice (yellowing) and bruising of the skin related to liver disease (Photograph courtesy RD Schultz, LJ Larson).

Immune complexes (combinations of antigen and antibody) may affect the kidneys and the eyes, leading to a transient **corneal opacity** ('**blue eye**').



Corneal opacity ('blue eye') developing as a consequence of an immune system reaction to CAV-1 infection (Photograph courtesy LE Carmichael).

Canine adenovirus type 2 (CAV-2) causes a usually **inapparent or mild to moderate infection of the respiratory tract** although severe pneumonia has been observed with death in untreated dogs. The virus is one of the causes of '**kennel cough**' or **canine respiratory disease complex (CRDC)**. This complex may also involve infection with **canine parainfluenza 2**, ***Bordetella bronchiseptica*** and other bacteria (e.g. *Streptococcus* and *Mycoplasma* species). Additionally, other environmental factors such as ventilation, humidity, dust, poor hygiene and particularly stress are important in development of this complex disease.

Canine Parvovirosis

The **canine parvovirus type 2** (CPV-2) is closely related to **feline parvovirus** (FPV; also known as feline panleukopaenia virus), from which it differs in only two amino acids in one protein. CPV-2 most likely originated from the cat virus by **mutations** in the late 1970s when it first appeared in dogs in the USA and then rapidly spread throughout the world. While the early variants were restricted to dogs and were

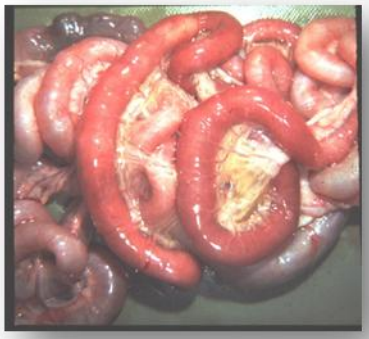
unable to infect cats, **virus evolution** (mutation) progressed and the more recent variants can cause enteric disease in cats that are not vaccinated against FPV.

Canine parvovirosis is a **common**, **worldwide enteric infection** of domestic and wild dogs of all ages (usually 6 – 16 weeks). **Puppies < 6 months of age** are the most severely affected. **Subclinical infections** are common, especially in older dogs (> 1 year of age). The virus is **shed in the faeces** and if it is **ingested or inhaled** by susceptible young dogs (< 1 year of age) it will infect and cause severe disease. Mortality can be as high as 50%, especially where treatment is not initiated immediately. Adult susceptible dogs may not necessarily develop disease; however, they will shed virus in their faeces and when susceptible pups (< 6 months of age) inhale or ingest this virus they often develop severe disease and many will die. Significantly, transmission not only occurs by direct contact but also **indirectly**, by **contaminated** shoes, clothing, materials (**fomites**). After **oronasal infection**, the virus **replicates in the tonsils and lymph nodes** and then **reaches the gut** in 4 – 6 days, destroying the intestinal epithelial cells leading to onset of diarrhoea 2 – 3 days later. Infection of a pregnant susceptible (unvaccinated) bitch may lead to infection of the fetus and result in heart disease (**myocarditis**). Similarly, myocarditis can occur in CPV-infected 1 – 2-week-old puppies. Therefore it is very important to ensure that bitches are vaccinated before breeding.

CPV-2 infection is one of the most lethal infections of the dog. The disease may occur suddenly, with death ensuing one or two days after clinical signs first appear. Commonly the disease develops more slowly, but still with an average mortality of up to 50%. Clinical signs include **inappetence**, **depression**, **fever**, **vomiting** and **diarrhoea** (**frequently bloody**). Severely affected dogs rapidly become

dehydrated, and without **electrolyte replacement therapy** die quickly; within 1 – 3 days after onset of clinical signs.

Vomiting in a dog with CPV-2 infection (Photograph courtesy LE Carmichael).



The intestines of a dog with CPV-2 infection. The red colour indicates severe inflammation (Photograph courtesy LE Carmichael).

Severe bloody diarrhoea in a dog with CPV-2 infection (Photograph courtesy RD Schultz, LJ Larson),

Sick dogs should be **isolated** immediately from other dogs. All parvoviruses of dogs and cats **remain infectious** for **at least a year** in contaminated cages and kennels, or on rugs, towels, grass or soil etc. Thorough **disinfection** (e.g. using sodium hypochlorite [bleach] solution) is necessary before new animals are admitted to the premises. When soil, grass, rugs, etc. are contaminated, disinfectant is often not effective or cannot be used. Therefore, the environment remains infected for months or possibly more than a year. Studies have shown that infectious CPV-2 may persist in soil for up to 1 year, where it remains capable of causing infection in susceptible dogs. The solution to introduction of new dogs is to be certain they are vaccinated and have developed antibody. If they are not vaccinated, they are likely to get infected and die.

Feline Parvovirus (Feline Panleukopenia)

This is the classical, severe virus disease of cats. It has also been known as **feline infectious enteritis**, and erroneously termed '**feline distemper**', '**cat flu**' or '**cat fever**'. It is caused by the feline parvovirus (FPV), which is likely to be the ancestor virus of the parvoviruses of dogs, mink and raccoons. FPV infects **domestic as well as exotic cats**, but also **raccoons**, **mink**, **foxes and other wildlife species**. Some dog parvovirus variants may also infect cats. When FPV is introduced into a community of unvaccinated cats, it can cause disease and death in a high percentage (> 50%) of the cats, especially when they are less than one year of age.

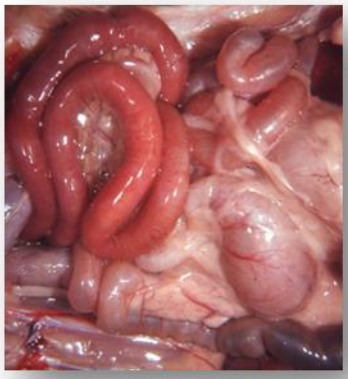
As explained above for the canine virus, this is one of the hardiest infectious agents known - it may **survive in the environment for years** and is **highly resistant to many current disinfectants**. Formaldehyde and bleach are necessary to eliminate it from contaminated premises. Obviously this is impossible in a home, which - once

contaminated - will harbor the virus for years. The solution is to only introduce vaccinated cats into such an environment.

Sick cats shed the virus at high concentrations **in the faeces**, which are the source of transmission via **oral or nasal uptake**. **Indirect contact** is the most common route of infection, and FPV may be carried even into homes in high-rise buildings on shoes and clothing by contaminated visitors. This means that **indoor cats are also at high risk of infection**. In pregnant queens, the virus can **pass through the uterus into the fetus**, and infection of neonates may occur. Not all of these kittens necessarily die, some may be born alive, but they will show neurological signs - conspicuous uncoordinated movements (**cerebellar ataxia** syndrome).

Cats of all ages may fall ill, but **kittens are most susceptible**. This is a deadly infection and the **mortality rates** may surpass 90% in some outbreaks, especially when young susceptible kittens are infected. Depending on the infected organs, disease signs are **diarrhoea** and **blood changes** (lymphopenia, neutropenia, followed by thrombocytopenia and anaemia). The scientific term '**panleukopenia**' indicates that all white blood cell types are reduced in number. Since these cells are important in the immune defence, the infection leads to **immunosuppression** and makes the infected cat more susceptible to other (often bacterial) infections.

A weak and depressed kitten with FPV infection (Photograph courtesy FW Scott).



The intestines of a kitten with FPV infection. The red colour indicates severe inflammation (Photograph courtesy FW Scott).

Evidence of profuse vomiting and diarrhoea in a severely ill kitten with FPV infection (Photograph courtesy RD Schultz, LJ Larson).

The veterinarian will use special tests to detect the virus in the diarrhoeic faeces. Either feline or canine parvovirus test kits may be used because the two viruses are closely related. In some countries, laboratories perform **polymerase chain reaction** (PCR) testing on whole blood or faeces. The PCR test is very sensitive and if a cat has been vaccinated recently it may be positive on testing.

Tender loving care by the owner is the secret to management of this disease. Supportive therapy and good **nursing** significantly decrease mortality rates. In cases of intestinal disease (diarrhoea), administration of a **broad-spectrum antibiotic** against bacteria is routine, to prevent sepsis. Confirmed cases, but also suspected animals, should be kept in **quarantine**. **Disinfectants** containing sodium hypochlorite (bleach), peracetic acid, formaldehyde or sodium hydroxide are effective, as mentioned above.

Feline Upper Respiratory Disease (Feline Viral Rhinotracheitis - Herpesvirus infection)

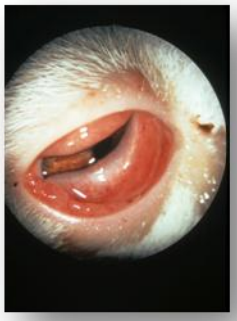
Upper respiratory disease in cats may be caused by several viruses, amongst which **feline herpesvirus type 1** (FHV-1) is most important and may result in fatal infections. The virus has a **worldwide distribution** and also occurs in **non-domestic cats**. It often occurs in association with **feline calicivirus** (FCV) and bacterial infection. FHV-1 remains **latent after recovery**, and most cats become **lifelong virus carriers**. Stress or immunosuppressive corticosteroid treatment may lead to **virus reactivation and shedding** leading to infection and disease in unvaccinated cats, especially young kittens.

Sick cats shed FHV-1 for up to 3 weeks in oral, nasal and conjunctival secretions. In contrast to FPV infection, FHV-1 infection requires **direct contact with a shedding cat**. It is common in **multi-cat situations** like boarding and breeding catteries, shelters and multi-cat households. Kittens may be infected **subclinically** by their **latently infected mothers**.

Clinical signs include acute **rhinitis** and **conjunctivitis**, usually accompanied by **fever**, **depression** and **anorexia**, which are particularly severe in young kittens; fatal **pneumonia** may occur, as well as an **ulcerative**, **dendritic keratitis**. Clinical signs usually resolve within 1 – 2 weeks.

Nasal discharge in a cat with FHV-1 infection (Photograph courtesy FW Scott).

Discharge from the eyes in a cat with FHV-1 infection (Photograph courtesy FW Scott).



Severe reddening and swelling of the conjunctiva (conjunctivitis) in a cat with FHV-1 infection (Photograph courtesy FW Scott).

Supportive **(fluid) therapy** and good **nursing care** are essential. Anorectic cats should be fed blended, highly palatable, warmed-up food. **Nebulization** with saline may offer relief. **Broad-spectrum antibiotics** are given to prevent secondary bacterial infections and **topical antiviral drugs** may be used for the treatment of acute ocular disease. Antibiotics and antiviral drugs should only be used under the direction of your veterinarian.

In shelters, new cats should be quarantined for 2 weeks. In breeding catteries, queens should kitten in isolation and the kittens should not mix with other cats until vaccinated. The herpesvirus is quite **labile** and **susceptible to most disinfectants**, **antiseptics and detergents**.

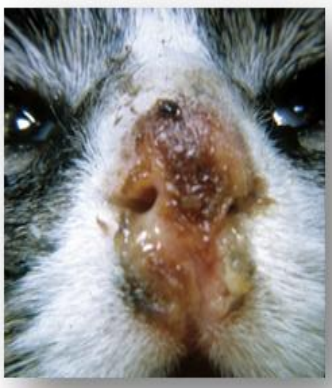
Feline Upper Respiratory Disease (Calicivirus Infection)

Feline caliciviruses (FCVs) are the other major agents responsible for feline upper respiratory disease. These are **highly contagious pathogens**, widespread among cats (including exotic cats) with the highest prevalence in **large groups of cats housed together**. The caliciviruses are **highly variable** and **mutate continually**:

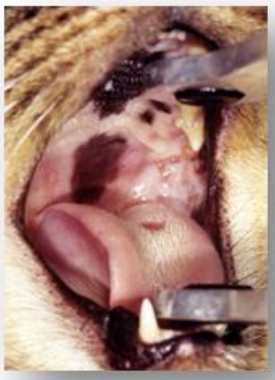
numerous variants exist, with a wide spectrum in **virulence**, **antigenic properties** and induced immunity. **Severe, systemic forms** of the infection causing a **haemorrhagic fatal disease** have been observed recently. Simultaneous infections with FHV-1, *Chlamydophila* and/or *Bordetella* often occur.

Sick, acutely infected or carrier cats **shed FCV in oronasal and conjunctival secretions**. Infection occurs mainly through **direct contact**, but **indirect transmission** is common, as the virus can **remain infectious on dry surfaces for about a month**. Feed dishes, water bowls, pet toys and other objects often become contaminated and can spread virus among cats in multi-cat households.

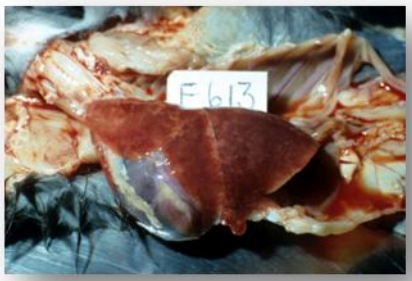
Clinical signs are predominantly **oral ulcers**, but caliciviruses also contribute to upper respiratory symptoms; fever as a sign of virus spread through the blood stream, and limping as a consequence of a **transient arthritis** may also be observed. **Pneumonia** occurs particularly in young kittens. The clinical picture depends on the virulence of the virus variant involved and the age of the cat.



Severe ulceration and crusting of the nose of a cat with FCV infection (Photograph courtesy FW Scott).



The red patch on the upper surface of the tongue of this cat is a deep ulcer caused by FCV infection (Photograph courtesy FW Scott).



In this kitten, severe FCV infection has spread to the lungs leading to death from pneumonia. The lungs are deep red in colour and would be consolidated. Normal lungs are soft and salmon-pink in colour (Photograph courtesy FW Scott).

A newly recognized form of this infection is **virulent systemic haemorrhagic FCV disease**, which is more severe in adult cats and fatal in up to about 70% of the cases. These patients show **fever**, **cutaneous oedema**, **ulcerative lesions** on the head and limbs and **jaundice**.

Supportive therapy (including fluid administration) and good nursing care are essential. The management of sick cats is the same as in cases of herpesvirus infection.

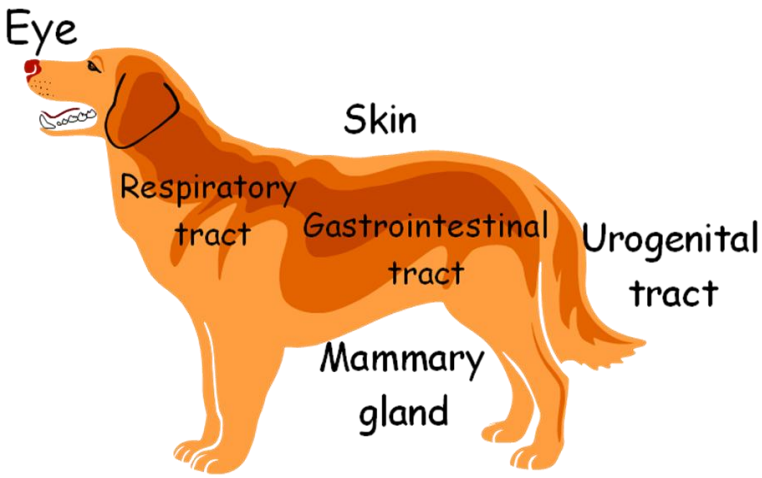
Caliciviruses can **persist in the environment** for about **one month** and are **resistant to many common disinfectants**. Sodium hypochlorite (bleach) is an effective antiseptic. In shelters, new arrivals should be **quarantined** for 2 weeks; in infected breeding catteries, queens should kitten in isolation and the litter should not mix with other cats until vaccinated.

THE IMMUNE RESPONSE

The immune system is a remarkable and intricate part of the body that is designed fundamentally to protect the individual from infectious disease. The immune system has developed throughout evolution in parallel with the development of infectious agents such as those described above. Therefore, in order to effectively deal with the myriad of infectious agents that now exists; the immune system has become very complex and specialized in mammalian species. The immune system must be able to respond appropriately to challenge with the whole spectrum of bacterial, viral, fungal, protozoal and nematode parasites. Many of these infectious agents have developed strategies to attempt to avoid the immune response so that they may survive and cause clinical disease or mortality in the hosts that they colonize. These strategies may be as simple as 'sneaking under the radar' of the immune system or be more sophisticated where some infectious agents can specifically subvert host immunity to their own benefit. Some knowledge of the immune system is required in order to understand why we vaccinate ourselves and our domestic animals.

There are two basic halves to the immune system – and these are called **innate** and **adaptive** immunity. The **innate immune system** comprises a group of white blood cells (**leucocytes**) and various protein molecules that are **immediate** and **non-**

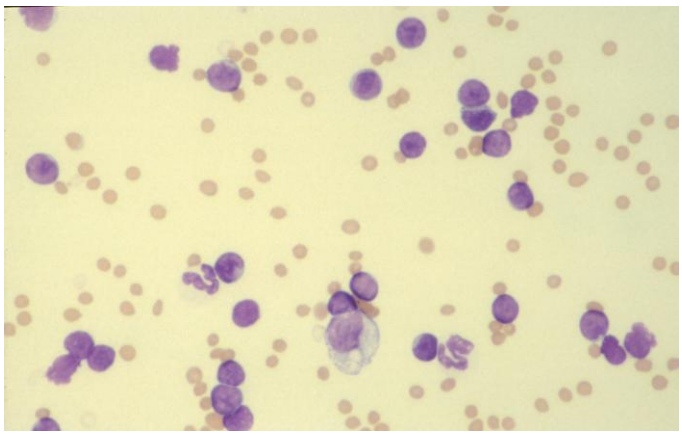
specific in their action. The innate immune system is often regarded as relatively primitive and in evolutionary terms is older than adaptive immunity – but nonetheless effective innate immunity is essential for survival of any animal. The components of innate immunity are most strongly represented at the **outer edges of the body** that are in most direct contact with the external environment. These include the skin, the mucosal surfaces of the respiratory, intestinal and urogenital tracts, the conjunctiva of the eye and the mammary gland. Any infectious agent is going to enter the body through one of these routes – for example by being inhaled (e.g. influenza virus) or ingested (*Salmonella* bacteria), so innate immunity is the **first line of defence** that helps exclude these organisms and prevent them from entering and sometimes spreading throughout the body. Although a crucial part of body defences, most vaccines do not act by stimulating innate immunity, but rather have their effect on the adaptive immune system.



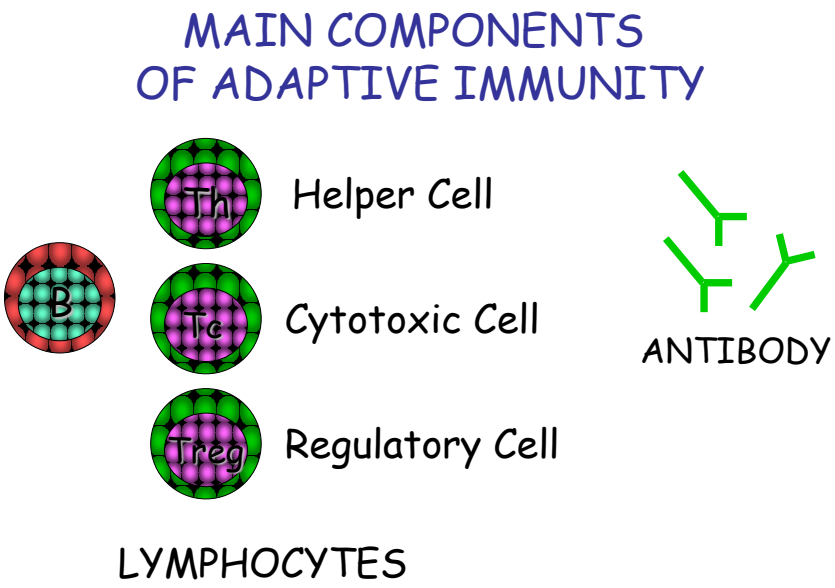
SITES OF INNATE IMMUNITY

Adaptive immunity is the second arm of host defence. The adaptive immune system is much **more powerful** than the innate and relies on a separate set of leucocytes and protein molecules. An important feature of adaptive immunity is that

these cells and proteins act in a **specific** fashion to target the particular infectious agent that has activated them. The key components of the adaptive immune system are the **lymphocytes** (cells) and **antibodies** (proteins). Some lymphocytes (B lymphocytes) are responsible for the production of antibodies whilst others (T lymphocytes) control or 'regulate' the adaptive immune response or undertake the process known as **cell-mediated immunity** (CMI). The lymphocytes of the adaptive immune system are found throughout the body. Some of these cells are located at body surfaces but most are present in particular **immunological organs** (the spleen and lymph nodes) and also circulate in the **bloodstream**.



The small orange-red cells in this picture are red blood cells. Most of the larger, blue-purple cells are lymphocytes – the cells responsible for the adaptive immune response (Photograph courtesy MJ Day).



When an infectious agent first enters the body it is held at bay by the innate immune system, which is always functional at body surfaces. Some days later the adaptive immune system is activated producing cells and antibodies specifically designed to counteract that organism. These very powerful immune players then come to provide 'reinforcements' to the innate immune system in order to help control or eliminate the infection. In many infections there is a role for both antibody and CMI in this protective immune response. Antibody can bind to and neutralize or destroy infectious agents, preventing them from entering or spreading within the body. Specific T lymphocytes, called 'cytotoxic T cells' can work with the 'natural killer' (NK) cells of the innate immune system to kill off body cells that are infected, thereby preventing spread of infection.

In addition to being more potent and specific, the adaptive immune system has one other key feature – that of **immunological memory**. At the conclusion of any immune response, some long-lived lymphocytes retain the memory of that infection, so if the same organism attempts to infect the body again in the future, those cells

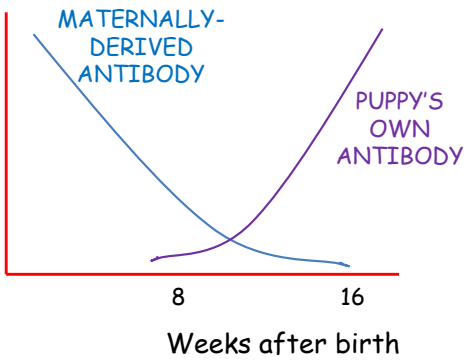
are rapidly activated to mediate an even more powerful '**memory immune response**'.

Vaccination therefore is a process by which exposure to a harmless form of an infectious agent (an 'attenuated' or 'killed' form of the agent) leads to generation of an adaptive immune response, and most significantly, to generation of a memory immune response. This will be further discussed in the next section.

At this point it is relevant to consider some other aspects of immunity that impact on vaccination. We increasingly realize that the effectiveness of the immune system of any one individual is under **genetic control**. As we are now able to dissect the entire genome (genetic makeup) of humans, dogs and most recently cats, we are beginning to understand which genes are important in controlling immune function. In fact for many years a group of 'immune response' genes has been recognized and shown to control adaptive immune responses. Humans and animals inherit different forms (alleles) of these genes which means that any one individual might respond differently to an infection or to a vaccination. For dogs, the genetic control of immunity is best demonstrated by comparing different breeds. We now understand how the creation of modern dog breeds by selective line-breeding has also led to a relatively restricted gene pool within these breeds. Particular breeds may have perpetuated genes related to weaker immune responses (or vaccine responses) as linked genes were selected to determine a particular body conformation. It is well known for example that some populations of Rottweiler dogs carry genes that mean they are unable to make protective immune responses (or vaccine responses) to canine parvovirus infection and some Rottweilers also make suboptimal immune responses to rabies virus vaccination.

The second key feature of the immune system of dogs and cats that impacts on vaccination is the process by which **newborn animals** are protected from infectious disease. Unlike in man where the newborn receives protective pre-formed antibodies from the mother by placental transfer, newborn pups and kittens (that have a more complex placental barrier than in man) must receive these maternal antibodies by taking in the 'first milk' or **colostrum** from the mother. These maternal antibodies are absorbed during the first few days of life and provide systemic immune protection for the neonate during the first weeks of life whilst their own immune system is becoming established. Without this **maternally-derived antibody** (MDA) the neonatal animal will rapidly succumb to infection and may die.

However, although essential for survival, the presence of MDA also prevents that young animal from making their own immune response – and in particular from responding to conventional vaccines. These maternal antibodies have a finite life span (the 'half life') and so eventually degrade away allowing the young animal to replace MDA with antibodies that it produces itself. Only when the MDA has sufficiently degraded is that young pup or kitten able to generate its own protective memory adaptive immune response to a vaccine. This is one of the reasons that we do not vaccinate pups and kittens for some weeks after they have been born.



This simple graph shows the decline in maternally-derived antibody (MDA) in the blood of a newborn puppy over the first weeks of life. Only after this antibody has dropped to a very low level can the puppy produce its own antibodies. In this example the puppy cannot make its own antibody (i.e. cannot respond to vaccination) at 8 weeks of age as there is too much MDA present. However by 12 and 16 weeks of age there is no longer an inhibitory concentration of MDA and the puppy could respond to vaccination.

This situation becomes slightly more complex if one considers that within a litter of pups or kittens the different individuals will likely absorb different amounts of maternal colostrum. The stronger animals may receive relatively more MDA than a small or weaker littermate that is pushed to the 'end of the line' for colostral uptake. Essentially, this means that individual animals within a litter become capable of responding to vaccination at different times – depending upon when their MDA was sufficiently degraded to permit their own antibody response. The runt of the litter that received relatively less colostrum might be capable of responding to vaccination at 8 weeks of age, whilst the more robust animals may still have persisting MDA blocking their own immunity until 12 weeks of age. That is why we recommend the last dose of core vaccines for kittens and pups be given at 14 – 16 weeks of age (see next section).

The **vaccination schedules** developed for pups and kittens therefore take into account this potential difference between littermates and between litters (as the antibody level for one dam may be dramatically different to another). Because we do not routinely test dams for antibody levels or the level of MDA in an individual pup or kitten, repeated vaccination is given (refer section below but generally starting at 8 – 9 weeks, with a second injection 3 – 4 weeks later and a third between 14 – 16 weeks). The runt of the litter may well respond to vaccination at 8 weeks (and is not harmed by receiving additional vaccination at 12 and 16 weeks), but the more robust littermate that gets more MDA may not be able to respond until 14 weeks of age. Furthermore, some entire litters born to a dam with a very high titre (e.g. to CPV-2) have no pups in the litter that develop an immune response until they receive the dose of vaccine given at 14 –16 weeks of age. The doses at 8 and 12 weeks will be completely blocked (see section on Vaccine Guidelines). The vaccination schedule consists of this initial '**priming**' of the adaptive immune response (that might occur at either 8, 12 or 16 weeks in any one individual) but also crucially includes revaccination at 12 months of age or at 12 months after administration of the 14 –16 week vaccination. Pups and kittens will benefit from this 12 month revaccination.

THE PRINCIPLE OF VACCINATION

The introduction of vaccination to the western world is largely attributed to the pioneering work of Edward Jenner, who in 1796 demonstrated that exposure to the cowpox virus could protect from subsequent challenge with the related smallpox virus. In the ensuing two centuries vaccination has become a cornerstone of both human and veterinary medicine. The importance of human vaccination to mankind is exemplified by the fact that smallpox no longer exists as a disease because of

vaccination programmes. A similar or perhaps greater vaccination achievement will occur in 2011 in veterinary medicine, where due to vaccination, the world will be declared free of bovine Rinderpest infection. Rinderpest virus is closely related to human measles and to canine distemper virus.

Major infectious diseases of dogs and cats (refer above) have also been effectively controlled (but not eliminated) by vaccination programmes over the past decades. Where vaccination is widely practiced in a population, killer diseases such as canine distemper, canine adenovirus and canine and feline parvovirus infections are relatively rare occurrences. To achieve effective control of these diseases, 50% or more of the animal population should be vaccinated at least once after the age of 14 – 16 weeks with an infectious (modified live) vaccine. Vaccination also prevents animal suffering by controlling infectious agents that do not necessarily kill the animal but do cause clinical signs (e.g. feline upper respiratory tract disease). Of course, in countries where vaccination is not widely practiced (i.e. in < 10% of the population), these diseases remain just as prevalent as they always have been.

So the **purpose of vaccination**, as we currently practice it, is to **protect individual animals and populations of animals from lethal or disease producing infections**. Although this is generally done for the benefit of the animal, for some infections that are shared with man (e.g. rabies) control of the disease in the animal population is a major means of preventing human infection. In this context, for rabies vaccination, there are often **legal requirements** associated with vaccinating pet animals – for example in countries where the disease is active ('endemic areas') or in the case of international pet travel.

Just as in human medicine, vaccination is not all just about the protection of the individual animal, but of the population as a whole. Recent debate about the vaccination of children with combined measles, mumps and rubella vaccines (in some countries) has led to a suboptimal number of the human population being vaccinated for these infectious diseases. When the population level of immunity (the '**herd immunity**') falls below 65%, there is a risk of outbreaks of that infectious disease. This has been clearly seen in the UK with recent outbreaks of measles virus infection in children. The same issue affects our companion animals, where for example, outbreaks of canine distemper or parvovirus have been linked to reduced uptake of vaccination. Vaccinating your pet therefore not only protects it from infection but is to the benefit of the entire animal population (see earlier discussion on approximate percentage of animals that need to be vaccinated to obtain effective population immunity).

As discussed above, vaccination is able to achieve this aim of controlling infectious disease by inducing a **memory immune response** in the **adaptive immune system**. The effectiveness of this memory response is determined by a number of factors such as the **genetic background** of the animal, the effectiveness (strength or '**potency**') of the vaccine, the persistence of immunity induced by the vaccine (the '**duration of immunity**' or **DOI**) and the **programme** by which the vaccine is administered. Some vaccines have been immeasurably successful in achieving their goal of inducing protection and a long-lived memory immune response (e.g. vaccines against CDV, CAV-2, CPV and FPV) whereas other vaccines, because of their nature, induce only short-lived immunity or may simply reduce the clinical signs of disease rather than preventing the actual infection (e.g. canine leptospirosis vaccines, canine and feline upper respiratory tract vaccines). Simply put, these less

effective vaccines must be given more frequently in adult animals (as '**booster vaccines**') in order to retain the immune response because memory persists for months rather than years.

The design of a vaccination programme for an individual pet animal is a **medical activity** that is best undertaken by your veterinarian. Although in this document we summarize the current **international guidelines** for canine and feline vaccination, in reality the vaccines that your dog or cat will receive, and the frequency in which they are administered, will be determined by factors such as the **infectious disease risk** in your country, region or local environment, the **lifestyle** of the animal, the **age** and sometimes **breed** of the animal, and the **nature of the vaccine** product that is selected. These factors and the approach to designing a vaccination programme for your pet are discussed in the sections that follow. A lifelong vaccination programme for an animal will include consideration of inducing protection in early life (by priming and boosting the immune response) and maintenance of protective immunity and immunological memory by periodical revaccination in adulthood (boosting).

TYPES OF VACCINE

There are two major types of canine and feline vaccines:

1. Infectious vaccines
2. Non-infectious vaccines

By definition, **infectious vaccines** must infect the animal to cause an immune response. In contrast, **non-infectious vaccine** cannot infect, and thus must contain an adequate amount of **antigen** to stimulate an immune response. Often the non-

infectious vaccines contain an **adjuvant**, which is a substance that non-specifically enhances the immune response.

Infectious vaccines are often referred to as **modified live vaccines** (MLV), or **live attenuated vaccines**. These vaccines stimulate all aspects of acquired immunity including cell-mediated immunity (CMI) and humoral (antibody) immunity, both systemically as well as locally. Therefore, infectious vaccines are often the most effective type of vaccines. They also induce the longest **duration of immunity** (DOI), ranging from years up to the lifetime of the animal. Often infectious vaccines require only one dose to immunize an animal when **maternally derived antibody** (MDA) is not present to prevent infection and block immunization. Infectious vaccines are most like the immunization that occurs after natural infection. The major difference is that natural infection often causes disease and sometimes death, whereas infectious vaccines do not as the infectious agents are **attenuated** (weakened) and thus are safe for use in animals of a specific species that has a fully functioning immune system. The **DNA vaccines**, also referred to as naked DNA vaccines, genetic vaccines, DNA vectors, recombinant DNA vaccines, or viral vectored recombinant vaccines, are most like the infectious vaccines because they can enter a cell and can be expressed by **antigen presenting cells** which will induce all forms of acquired immunity much like the infectious vaccines. The most important forms of acquired immunity are **humoral** (antibody) and **cell-mediated** immunity (see section on immunity above). The one form of immunity not readily induced by the parenteral (systemic) inoculation of a DNA vaccine, which is often stimulated by infectious vaccines, is local mucosal immunity.

Non-infectious vaccines are also referred to as **inactivated**, dead, killed, idiotypic, peptide, subunit, synthetic, toxoid, antivenom or bacterins. The non-infectious vaccine must contain enough antigen to immunize, as they do not infect nor do they produce new antigen. They often must also contain an adjuvant to non-specifically enhance the immune system. The non-infectious vaccines, unlike the infectious vaccines often:

- Require **multiple doses** to produce an immune response
- Provide a **shorter duration of immunity** than the infectious vaccines
- Stimulate primarily **systemic humoral immunity**, limited CMI and little or no mucosal immunity
- Are more likely to cause an immunological adverse reaction, especially when they include adjuvants or contain whole killed bacteria (bacterins). In the cat, non-infectious vaccines, especially those containing adjuvants, have been suggested to be one possible cause of the lethal cancer termed '**feline injection site sarcoma**' (FISS). The killed vaccines most often associated with FISS are killed adjuvanted rabies vaccines and killed adjuvanted feline leukemia vaccines.

Multiple types of vaccines are included in the vaccination programs for most animals, as even core vaccines may be non-infectious (e.g. rabies vaccine).

Vaccine immunity persists through the action of immunological **memory cells** and with certain types of vaccines (generally the infectious vaccines) immunity can persist for many years and up to a lifetime. A good example is measles vaccination in people. Childhood vaccination provides a lifetime of immunity (average human lifetime is 75 years). Canine distemper virus is very closely related to measles virus,

and the canine distemper vaccine can also provide a lifetime of immunity in the dog (average lifespan of 12 – 14 years). Canine parvovirus and feline panleukopenia virus also can provide lifelong immunity. It is important to understand that no type of vaccine can provide a longer DOI than the DOI which occurs after natural immunization (the immunity conferred after an animal recovers from natural infection, with or without disease).

In contrast, there are some vaccines that are unable to provide the same DOI as natural immunization (e.g. *Leptospira* vaccines). Those vaccines are most often non-infectious. In general, DOI to viruses is longer than immunity to bacteria or parasites. Also, immunity to viruses is often more complete; that is, immunity can sometimes even prevent viral infection, which is the ultimate form of immunity. This form of immunity is termed '**sterile immunity**' since infection does not occur, thus there can be no disease. Most vaccines, including certain viral vaccines, cannot prevent infection, but instead prevent disease or reduce the severity of the specific disease they are designed to prevent.

Some, but not all, of the infectious vaccines are shed after they are administered to an animal. For example, the canine and feline parvovirus vaccines are shed in the faeces of a recently vaccinated pup or kitten, respectively. The virus that is shed is the attenuated vaccine virus, therefore it would not be of concern if the shed virus were to infect other susceptible pups or kittens that have maternally derived antibody or are older than 2 weeks of age. However, breeders should be aware that if pups younger than 2 weeks that were deprived of colostral antibody are infected with the modified live CPV-2 that is shed from older vaccinated pups, or if they are vaccinated with CPV-2, the vaccine virus has the potential to cause damage to the

heart (myocardial inflammation). Although the MLV CDV vaccine is not normally shed, this virus could infect the brain if given to a colostrum-deprived pup less than 2 weeks old.

To prevent this from occurring, colostrum-deprived pups or CPV-2 antibody negative pups should not be given CPV-2 or CDV vaccines or any other core vaccines until they are at least 4 weeks of age. At or after 4 weeks of age it is safe to give the core vaccines, but unless pups or kittens are colostrum-deprived and/or they are in a high risk environment **we don't recommend starting the vaccination program for pet animals before 6 weeks of age**. The reasons for this advice are: (1) the vaccines may be blocked by MDA, (2) the pups and kittens are passively protected and they don't need to be vaccinated, and (3) their immune systems are more mature and are likely to produce a better protective immune response at 6 weeks of age or older.

When pups or kittens fail to receive colostrum the best method to provide protection is by using **artificial colostrum** or administering hyperimmune serum that has high levels of antibody to the core infectious agents. This approach can provide beneficial protection against CDV, CPV-2, CAV-1 in puppies and FPV in kittens.

A method that can be used by your veterinarian to make artificial colostrum is to take 50ml of a milk replacer (e.g. Esbilac or similar milk product) and add to it 50ml of immune serum from a well vaccinated dog/cat or from the bitch/queen of the orphaned pups/kittens if she is available. If the pups or kittens are 3 days of age or less and they have not received any protein orally, the pups can be fed the artificial colostrum for 3 days. The pups should then have the same or similar levels of antibody to the core viruses as they would have they received from the colostrum of

the bitch. If the pups are older than 3 days or if they have been given milk replacer orally, the immune serum would need to be injected intraperitoneally (IP) or subcutaneously (SC) by your veterinarian. It is also possible for your veterinarian to administer **plasma** intravenously (IV). The amount of serum or plasma to administer would be 3 – 10 ml depending on the size of the pup. The serum should be administered SC or IP, twice daily for up to 3 days. A similar procedure could be used for kittens. The puppies or kittens that receive the artificial colostrum or the serum treatments should be vaccinated with core vaccines starting at 6 weeks of age then revaccinated at 3 to 4 week intervals until they are 14 to 16 weeks of age to provide long lasting active immunity.

DRIVERS FOR CHANGE IN VACCINATION PROTOCOLS

What important factors have recently driven the veterinary profession to develop vaccination guidelines for the cat and dog? Feline vaccination guidelines were developed first by the American Association of Feline Practitioners (AAFP) in 1998 and updated in 2000 and 2006. Canine vaccination guidelines were developed by the Canine Vaccine Task Force, American Animal Hospital Association (AAHA) and published in 2003, 2006 and 2010. Guidelines for the vaccination of both dogs and cats were developed by the Vaccination Guidelines Group (VGG) of the World Small Animal Veterinary Association (WSAVA) in 2007 and 2010.

The AAFP was primarily driven to developing vaccination guidelines when it was suggested that vaccines might be associated with the development of malignant tumours at vaccine injection sites. Until that time the accepted practice was to give every vaccine available to all dogs or cats at least annually and preferably in a

combination product. It was also widely believed that vaccines could cause no harm. The tumours were originally referred to as vaccine-associated sarcomas (VAS); however, we now refer to them as feline injection site sarcomas (FISS). The word 'vaccine' was removed since injections with other substances can cause these sarcomas in highly predisposed cats. It is believed that anything causing a significant inflammatory reaction in the skin has the potential to cause FISS in high risk cats. Injection site sarcoma is primarily, but not exclusively, a problem in cats. Other species (e.g. ferret, dog and horse) may develop these tumours, but at a much reduced frequency compared with the cat. Genetic background is likely to play an important role in the development of FISS, but genetic factors have been poorly defined.

The two vaccines most frequently associated with FISS are adjuvanted, non-infectious (killed) feline leukaemia virus (FeLV) and rabies vaccines. In the USA, the prevalence of FISS is estimated to be 1 per 1,000 – 10,000 vaccinated cats. Some veterinary practices see FISS more often than 1 per 1,000 cats and other practices far less than 1 in 10,000. There are practices that have still never seen a case of FISS. In the UK, a prevalence of 0.021 cases per 10,000 vaccines sold was reported in 2001 and FISS continues to be recognized. In the UK cats only receive rabies vaccination as a condition of international travel, but FeLV vaccines remain widely used.

No single adverse event like FISS was the driver for the development of canine vaccination guidelines. Instead, it was growing awareness that many vaccines provided a long duration of immunity (DOI) and therefore did not need to be administered yearly. Of course adverse reactions do occasionally occur following

vaccination of dogs. Canine adverse reactions include relatively mild allergic events like hives, facial oedema and urticaria occurring within minutes to hours after vaccination. Whilst these reactions are readily related to preceding vaccine administration, it is more difficult to define the adverse reactions that occur a day, a week or months after vaccination. Adverse reactions will be further discussed in a subsequent section of this document.

CANINE VACCINATION GUIDELINES

Dog breeders have a special role to play in assuring that the puppies they raise and sell are properly vaccinated. The initial series of vaccines administered by the breeder (this is only possible in some countries) or their veterinarian almost always requires that the new owner continue the vaccination series to ensure the puppy is protected against the important diseases at an early age and throughout their lifetime. It is critically important that the breeder provide information, preferably **veterinary records**, of what vaccines the puppy has received. Copies of those records should be given to the new owner so that they can be shared with their veterinarian. This will ensure that the series of vaccinations continues and that the vaccination programme is adequate to provide the protection required.

The most important canine diseases based on **morbidity** (severity of disease signs) and **mortality** are the three 'core' diseases: (1) canine distemper caused by **canine distemper virus** (CDV), (2) canine parvovirosis caused by **canine parvovirus type 2** (CPV-2), and (3) infectious canine hepatitis (ICH) caused by **canine adenovirus type 1** (CAV-1). In many countries, the vaccine used to prevent ICH contains canine adenovirus-2 (CAV-2). In addition to these three core diseases that are found worldwide, dogs in many, but not all countries, should also be vaccinated with **rabies**

vaccine to prevent infection of the dog as well as human beings and other species, wild and domestic, with rabies virus. The vaccines that prevent these four devastating diseases are referred to as the **core vaccines**. The type of core vaccines that should be given to puppies to prevent disease caused by CDV, CPV-2 and CAV-1 are the infectious vaccines, also referred to as modified live viral (MLV), vaccines (see Types of Vaccines above). In some countries a **viral vectored recombinant** (r)CDV vaccine is available and may be given instead of the MLV CDV vaccine. When available, MLV-CAV-2 vaccine should be used rather than MLV CAV-1 to prevent ICH caused by CAV-1. The CAV-2 is as effective as the CAV-1 vaccine, but the CAV-2 vaccine will not cause the adverse reaction known as **blue eye** (allergic uveitis), that can be produced by CAV-1 vaccines. Under no circumstance should a non-infectious (killed, inactivated) vaccine be used during the puppy series to replace the MLV vaccines or the recombinant (r) viral vectored vaccine when these products are available. In contrast, the rabies vaccines given to animals should only be non-infectious (killed, inactivated) products or the infectious viral vectored recombinant feline rabies vaccine that is available in some countries.

Vaccinations with the three **core canine vaccines** (CDV, CPV-2 and CAV-2) should not begin earlier than 6 weeks of age and if the puppies are to remain with the breeder until they are 8 – 10 weeks or older, it is recommended that vaccination **begin at 8 – 10 weeks rather than 6 weeks**. Revaccination should be 3 – 4 weeks later with a final vaccination given when the pups are 14 – 16 weeks of age. The ability to immunize the puppies will depend on the antibody titre of the dam and the amount of **maternally derived antibody** (MDA) that is absorbed via specialized epithelial cells in the intestinal tract of the puppy during the first 24 – 72 hours after birth. After MDA absorption of the canine IgG antibody has been completed there is

gut closure and no additional IgG antibody will be absorbed. This occurs during the first 2 – 3 days of age (see earlier sections). **Milk antibodies**, primarily of the IgA class, but also some of the IgG class, will continue to provide **local mucosal protection** of the gastrointestinal (GI) tract until the puppy is weaned. Although passive immunity in the GI tract is important against enteric pathogens, the most important passive (maternal) protection from diseases is the IgG antibody in the blood of the puppy.

The **passively acquired immunity** (MDA) provides protection against many of the infectious agents to which the dam has been exposed (by vaccination or natural exposure) and to which she has developed antibody (e.g. CDV, CPV-2, CAV-1, CAV-2, rabies, other systemic diseases such as canine herpes virus). Unfortunately, the passive IgG antibody that provides temporary protection for the pup also prevents active immunization (see earlier sections) when the core vaccines are administered parenterally (intramuscularly [IM] or subcutaneously [SC]) to the puppies.

The **passive IgG antibody** in the blood of the puppy has an average **half-life of 10 days** (range 8 – 12 days). That means, depending on the pup, every 8 – 12 days, one half of the antibody passively transferred from the mother to her pup to help prevent infection by CDV, CPV-2, CAV-1, rabies virus or other pathogens decays (disappears). Thus, depending on the antibody titre of the dam, all or most of the **passive protection** will generally be gone between 6 – 16 weeks of age. The protection from each pathogen (virus, bacteria) is dependent on the amount of MDA to that pathogen so, for example, the protection from CDV infection may last to 8 weeks of age, whereas protection from CPV-2 may last for 12 weeks and protection

from CAV-1 may be for 14 weeks. However, every dam will be different, depending on her antibody titres, but all the pups in the litter of a given dam will generally have similar, but not identical, antibody titres, provided they all received colostrum during the first 3 days after birth (see earlier section on the Immune Response).

For the example above, the dam has a low CDV titre and a high CPV-2 and CAV-1 titre, thus all the pups should also have a low CDV titre and high CPV-2 and CAV-1 titres. What that means regarding passive protection is that the pups will be susceptible to infection with CDV at an early age (e.g. 8 weeks) and to CPV-2 and CAV-1 at an older age (e.g. 12 – 14 weeks). It also means that these specific pups can be immunized at an early age (e.g. 8 weeks) with CDV, whereas they can't be immunized with CPV-2 and CAV-1 vaccines until 14 or more weeks of age. If these pups are vaccinated starting at 6 weeks of age, they would not develop immunity to CDV, CPV-2 or CAV-1. If they are vaccinated at 8 or 10 weeks, they should develop immunity to CDV. However, CPV-2 or CAV-2 vaccination at that time will provide **no immunity** nor will a vaccination administered again at 11 – 12 weeks provide any immunity to CPV-2, CAV-2 or CAV-1. In this example, the dose of vaccine given at 14 weeks or older should immunize all of the pups against CPV-2 and CAV-1, thus they will be immune to these three diseases.

Therefore, the **multiple doses of vaccines** are given not because MLV vaccines require multiple doses to immunize. Instead, they are given multiple times to ensure they are given when the passive antibody to that specific vaccine virus has declined to a level that won't neutralize (inactivate) the vaccine virus. The **vaccine virus must infect the dog to provide immunity**. When the MDA is high enough to block immunization with the infectious (modified live viral) vaccines, it is necessary to wait

at least 2 weeks to readminister the vaccine. Since half of the passive antibody will decay (disappear) during that time period, the level may become low enough to not block active immunization and the pup will become immunized. When the antibody titre of the dam is known for each of the core diseases, it is possible to predict the ages at which the litter of pups can be actively immunized with specific core vaccines. In the 1960s and 70s the age of immunization was often determined by a nomograph. However, this is rarely done today because of the high costs involved in testing and simply administering a series of vaccinations is more practical. The recommendation is to start vaccination at 6 – 8 weeks and to revaccinate every 3 – 4 weeks with the last dose at 14 – 16 weeks of age.

From a purely disease prevention perspective, it would be ideal to keep the pups isolated from other dogs with an unknown history of disease until the pups are actively immunized (e.g. their vaccination programme is complete), but that is rarely possible. It is also undesirable from many other perspectives, such as **socialization**, **training**, sales etc. Revaccination, regardless of the type of vaccines, should not occur more often than every 2 weeks during the period from 6 – 16 weeks of age. Ideally, there should be no more than three doses of core vaccines administered to a given pup during the early neonatal period. Examples of vaccination programmes for pups would be vaccination at 6, 10 and 14 weeks or 8, 11 and 15 weeks or 9, 12 and 15 weeks or 8, 12 and 16 weeks. When the first dose of the vaccine is given at 16 weeks of age or older, only one dose is generally needed because there is almost no likelihood that MDA would prevent active immunization. However, even when vaccination begins at 16 weeks of age, we often recommend two doses, 2 or more weeks apart, as there are a small percentage of pups that don’t develop a response for whatever reason to a specific infectious MLV

vaccine with only one dose. It must be understood that only the infectious MLV or recombinant viral vectored CDV, and MLV CPV-2 and CAV-2 core vaccines will immunize using only one dose.

The **non-infectious/killed/inactivated vaccines** almost always require two or more doses, which are usually given 2 – 6 weeks apart to produce immunity. If more than 6 weeks has passed since the first dose, the vaccination protocol should be repeated, making certain the second dose is given not more than 6 weeks after the first dose. An exception to this rule is the rabies vaccine, where a single dose will immunize due to the strong protective antigen (glycoprotein G) and the powerful adjuvant. However, even with rabies a second dose at up to 1 year after the first is required to ensure continued protection.

It is often asked: why not just wait until pups are 14 – 16 weeks of age to vaccinate for the core diseases? It would be possible if the pups were isolated; however, because certain puppies would be susceptible from as early as 6 weeks of age, if their dam had very low levels of antibody, waiting to vaccinate until 14 – 16 weeks would provide a very wide window of susceptibility (e.g. 8 – 10 weeks) and if they were infected with CDV, CPV-2 or CAV-1, they could get sick and would very likely die. However, if you kept the pups in an environment where you could ensure they wouldn't get infected with CDV, CPV-2, or CAV-1 then you could wait until 14 – 16 weeks or older to vaccinate with one or two doses of the core vaccines including rabies, which can be given as early as 12 weeks of age. **Rabies vaccines**, when required, must be given according to the local county, city, province, state or country **regulations**. The longest minimum DOI for any canine rabies vaccine tested to date

is 3 years. However, studies are in progress to determine if a vaccine with a much longer minimum DOI (e.g. 5 – 7 years) can be found.

The MLV CDV and rCDV, as well as the MLV CPV-2 and CAV-2 vaccines can provide **up to a lifetime of immunity** when one or, preferably, two doses are given in the absence of MDA. For the core vaccines (CDV, CPV-2, CAV-2), the VGG recommends revaccination at 1 year of age or 1 year after the puppy series ends, then **not more often than every 3 years**. For rabies, revaccination should be at 1 year or less and then every 3 years or less, depending on local regulations. In contrast to the long (many years) DOI for the core vaccines, the optional (noncore) vaccines generally provide only 1 year or less DOI. Also, unlike the core vaccines that are often 99% effective when the animal is properly immunized, many of the **non-core vaccines have an efficacy of 70% or less**.

The question is often asked: how long after vaccination does it take for immunity to develop when MDA does not interfere? Fortunately, the canine core vaccines are among the best vaccines available for any species. The immunity that protects from significant CDV disease when the MLV or rCDV vaccines are used is achieved in less than 3 days. The time for immunity to develop after CPV-2 vaccination is as early as 3 days, and one can regularly expect immunity from infection and/or disease in 4 – 5 days. Immunity to CAV-1 takes 5 – 7 days to develop. So within a week of vaccination in the absence of MDA, one can expect protection from diseases caused by CDV, CPV-2 and CAV-1. Immunity from the first dose of rabies takes at least 2 weeks and most dogs are not considered to be protected until 4 weeks after the first dose. A few dogs are not protected until a week or more after the second dose.

In addition to starting the first series of core vaccines at 6 – 10 weeks of age, the veterinarian (or the breeder in some countries) can, if desired, also give a kennel cough vaccine, which is a non-core vaccine. The VGG recommends an **intranasal vaccine** that includes modified live *Bordetella bronchiseptica* and canine parainfluenza virus, with or without CAV-2. Intranasal vaccines should only ever be given intranasally, as administration by any other route will cause a severe local or systemic reaction sometimes causing death. Since puppies will frequently only receive the first and possibly the second core vaccinations prior to sale, it is important that the breeder ensures that the new owner understands that it is essential that their veterinarian completes the vaccination series, with the last dose of core vaccines being given between 14 – 16 weeks of age or older. It is also incumbent on the owner to discuss the non-core (optional) vaccines with their veterinarian to determine the risks and benefits of all the non-core vaccines that are available.

The **non-core vaccines** can be started before or after completion of the core vaccines. Ideally the non-core vaccines would be given only when needed, starting two or more weeks after completion of the core viral vaccines. Many, but not all, non-core vaccines (e.g. those that protect from **leptospirosis** or **borreliosis** [Lyme disease]) require two doses administered 2 – 4 weeks apart because they are non-infectious (killed/inactivated) vaccines. In contrast to the core vaccines, which have a long DOI, most of the non-core vaccines must be given annually and sometimes more often for animals at very high risk of disease.

Thus, as a breeder, one of the most important roles you can play in ensuring the health of all dogs is to follow these guidelines for puppy vaccination, making certain

that all pups are vaccinated with the core vaccines at an age when they are able to develop immunity. It should be the goal of every dog breeder to not only have the best dogs, but to also have the healthiest dogs.

With regard to your adult breeding dogs, male and female, it is important to ensure they are vaccinated correctly with core vaccines, but that they are not over-vaccinated or receive unnecessary non-core vaccines. Every adult dog needs to receive the core vaccines, but they need not be given more often than every three years. We recommend that **no vaccines be given during pregnancy** as they are not needed and could cause problems (e.g. stillbirths, abortions, weak puppies). The exception to this would be where a vaccine is specifically licensed for use during pregnancy (e.g. the **canine herpes virus** vaccine that is available in Europe). When necessary, vaccination should be prior to or after pregnancy. Although it has been assumed that revaccination prior to pregnancy will boost the antibody level in the bitch so that she can transfer a higher level of the MDA to the pup, revaccination, especially with infectious/MLV vaccines, often provides no increase (boost) in her antibody because her existing antibody neutralizes the vaccine at time of injection, so it does not infect or cause an immune response, which is what is required to provide immunity and to increase the antibody level.

Almost all bitches, when revaccinated routinely every 3 or more years, will have an optimal **maintenance level of antibody** to the specific core virus they can develop. There is always a small percentage of bitches that will have very low antibody titres to one or more of the core viruses, and there will be a small percentage that will have very high titres to a specific pathogen, regardless of how often they are vaccinated (due to the genetics of their immune system). Because the responses are virus

(antigen) specific, an animal with a high level of antibody to CPV-2 may have an average or even a low level of antibody to CDV.

The level of response is also controlled by the **genetics** of the animal. In fact, there are a few animals that will be **non-responders** – that is, they are unable to develop antibody to the virus, regardless of how often they are vaccinated. It is estimated that the number of non-responders to CPV-2 is 1 per 1,000 dogs and to CDV is 1 per 5,000 dogs in the general population, but that number can be higher in a specific breed or family of dogs. Non-responders to CAV-1 or CAV-2 have not been found; therefore it is estimated that only 1 in 50,000 – 100,000 or more dogs may be non-responders to canine adenovirus. We don't know the percentage of non-responders to rabies virus, but we know they exist. The non-responders, if infected, will often die from the disease caused by the pathogen, to which they are unable to develop an antibody response (e.g. CDV, CPV-2). There are some breeders that recommend their pups not be vaccinated with certain vaccines. If those vaccines are non-core (optional), those recommendations may be acceptable. However, if they are core vaccines, not vaccinating is unacceptable. There should be no dog that does not receive the core vaccines (CDV, CPV-2, CAV-1 or 2) and rabies where it is required.

FELINE VACCINATION GUIDELINES

Cat breeders have a critical role to play in assuring that the kittens they raise and sell are properly vaccinated and remain healthy. There are core vaccines that all cat breeders and owners should give to their kittens, starting as early as 6 weeks of age, but preferably waiting until 8 – 10 weeks of age. The vaccines include the **feline (panleukopenia) parvovirus virus** (FPV) vaccine, the **feline calicivirus** (FCV)

vaccine, the **feline herpes virus-1** (FHV-1) vaccine and, in some countries, the **rabies virus** (RV) vaccine. Revaccination of the kittens should occur so that the last dose of vaccines is given between 14 –16 weeks of age. Therefore a two dose or three dose schedule can be used to ensure that all cats are protected from the diseases caused by these viruses. A two dose schedule, with **modified live vaccines** (MLV) would, for example, be at 8 and 14 weeks, or 10 and 14 – 16 weeks, whereas a three dose schedule could be 8, 12 and 16 or 10, 13 and 16 weeks. The intervals between doses of **MLV (infectious) vaccines** are not as restrictive as those between **killed (non-infectious) vaccines**. Two doses of killed vaccines are almost always required and the interval between those doses should not exceed 6 weeks, whereas when the first dose of an MLV vaccine is given, it should be at least 2 weeks before the second dose is given, but this period can exceed the 6 week maximum interval required for killed (non-infectious) vaccines. Although MLV vaccines are generally effective when only one dose is given in the absence of **maternally derived antibody** (MDA), some cats given the combination core vaccine require two doses to mount an antibody response to the FCV and/or FHV-1 vaccines. Therefore, a minimum of two doses is recommended, even when cats are first vaccinated at 16 weeks of age or older, at a time when the kittens no longer have MDA.

The FPV vaccines, especially the infectious (MLV) vaccines, are highly effective, having a 99% efficacy when the last dose is administered at 14 – 16 weeks of age. In contrast, the **efficacy is much less for the FCV and FHV-1 vaccines** (estimated at 60 – 80%), due to the nature of the viruses and the diseases they cause. Respiratory and other mucosal surface diseases, such as the **feline respiratory disease complex** (FRDC), are much more difficult to prevent than systemic

diseases like feline panleukopenia. The other core feline vaccine recommended for cats in certain, but not all, countries is rabies vaccine. When available, a modified live rabies virus can be used, but most rabies virus vaccines are killed adjuvanted vaccines or, in certain countries, a viral vectored recombinant rabies vaccine is available. When rabies vaccines are given, you must follow the regulations for your country as to when they should be given and how often they are required. **Revaccination** of cats with the core vaccines FPV, FCV, FHV-1 is recommended at **1 year of age or 1 year after the last kitten vaccines**, then **not more often than every 3 years**. Some veterinarians prefer to give the FCV and FHV-1 vaccines yearly because those vaccines are not as effective as the FPV. However, studies have not been done to show that yearly revaccination provides better protection than the triennial vaccination.

Two additional and very important infectious diseases of cats that could be significantly reduced, if not eliminated, through identification and elimination or isolation of carrier cats and vaccination of susceptible cats are feline leukaemia, caused by **feline leukaemia virus** (FeLV), and feline immunodeficiency disease, caused by **feline immunodeficiency virus** (FIV). Both of these diseases are caused by **retroviruses** that are found only in the feline species. Excellent diagnostic tests are available to detect '**carrier cats**' that serve as the primary source of infection for **susceptible cats**. If the carrier cats were eliminated, these diseases would disappear from the species. Therefore, it is essential that all cats used for breeding purposes be tested for FeLV using a reliable FeLV antigen detection test and for FIV using a reliable FIV **antibody test** or a **polymerase chain reaction (PCR) test**. Neither FeLV persistently infected (test positive) nor FIV infected (test positive) cats should be used for breeding. Furthermore, kittens born

to FeLV and FIV negative queens should not be housed where FeLV or FIV positive cats live or visit. The reason is that young kittens are highly susceptible to infection with both of these viruses. When young kittens are infected with FeLV, they have a high probability of becoming **persistently viraemic** (**carrier cats**) for life, thus serving as a reservoir for new viral infections. Furthermore, FeLV and/or FIV infected males should not be used for breeding purposes, as they can infect the queens and when the infected males are present in the household, they serve as an important source of infection for the newborn kittens.

Although FeLV vaccines are available in most countries and FIV vaccine is available in a few countries, elimination or isolation of the positive carrier cats will do more to prevent these diseases in the population than the vaccines alone. These vaccines are **not considered core** (e.g. vaccines every kitten should receive); however, **vaccination, especially with FeLV is highly recommended for kittens**. Vaccination should begin as early as 8 – 9 weeks, followed by a second dose (required for all FeLV vaccines) 2 – 6 weeks later. When the second dose is not given within 6 weeks of the first, two doses should be given, again making certain that the second dose is 2 – 6 weeks after the first. The FeLV vaccine should be given again **at a year of age** and then **not more often than every three years**. The FIV vaccine, even if available, is not recommended, because vaccination will interfere with the serological diagnostic test (e.g. make it positive), as this relies on antibody, and the PCR diagnostic tests available at this point in time are not always reliable. Furthermore, the FIV vaccine currently available is not proven to provide protection against all clades (strains) of FIV, thus even vaccinated cats can become infected and shed the virus.

With the virus testing and the core vaccination schedule suggested above, it would be expected that your cats should remain free of the vaccine preventable diseases for a lifetime. However, it is important to understand that FRDC is very complex and many things contribute to this disease. Thus, **FRDC is not vaccine preventable** and the best you can expect from the vaccines that are available (FCV, FHV-1 and others like ***Chlamydophila*** and ***Bordetella***) is **reduced severity of disease signs**. However, a vaccination program with the core vaccines and control and elimination of FeLV and FIV carrier cats will lead to a much healthier cat as well as a much healthier population of cats.

Adverse events from use of feline core vaccines are in general uncommon. The two most severe adverse events seen in the cat are **anaphylaxis** that, if not treated immediately with epinephrine (adrenaline), can be lethal, and **feline injection site sarcomas** (FISS) that are generally lethal whether treated or not. Both of these severe adverse reactions can occur at a prevalence of between 1 in 1,000 to 1 in 10,000 vaccinated cats. A cat with a history of anaphylaxis should not be revaccinated with the offending vaccines (if these are known). Affected cats with a history of this adverse reaction should be tested for antibody to FPV. When antibody is present to FPV, regardless of titre, the cat should probably not be revaccinated with any vaccines. Due to the high mortality associated with FPV disease, it is critical the cat is immune (antibody positive) for the FPV virus.

There are many types of feline vaccines available to prevent the core diseases. They include infectious (MLV/attenuated) vaccines and non-infectious (killed, inactivated) vaccines. Some of the infectious vaccines can be given **intranasally** and others are for **systemic (intramuscular or subcutaneous)** injection only. It is

critically important that the vaccine be given according to the manufacturer's recommendation on the label. If a MLV core vaccine that must be given systemically is given locally (e.g. intranasally or conjunctivally), the vaccine may cause disease. In contrast, a killed vaccine that must be given systemically and always requires two doses, if given locally will provide no protection. Both infectious (MLV) and non-infectious (killed) vaccines can be effective in preventing disease and both types are often used in vaccination programs. In general, **infectious core vaccines are the most effective** and they are **often the safest** as they are less likely to cause adverse reactions, especially hypersensitivity reactions and FISS compared with non-infectious (killed) vaccines.

Your veterinarian will provide the safest and most effective disease prevention programme for your cats, which will include vaccination with both infectious and non-infectious vaccines and diagnostic testing for diseases like FeLV and FIV to help eliminate these diseases.

REPORTING OF ADVERSE REACTIONS

As discussed above, the main driver for change in companion animal vaccinology over the past decade has been a desire to improve the already **very high safety level of vaccination**. There can never be a guarantee, in either human or veterinary medicine, that every single administration of a vaccine will be perfectly safe and without adverse consequences. There is a realization that on rare occasions, vaccination of a dog or cat might lead to an unexpected clinical reaction. Such reactions are for the most part mild and inconsequential and a simple **risk benefit analysis** will always suggest that the benefit obtained from having solid

immunity to potentially lethal disease far outweighs the small risk of a vaccine-associated adverse event.

Good **scientific data** on the prevalence of vaccine reactions in man and animals simply do not exist. The main reason for this relates to the fact that not all such events are recorded and so the true prevalence can only be a best estimate. The most powerful recent information has come from analysis of the computerized medical records of the North American Banfield Hospital Group which provide standardized clinical records for hundreds of veterinary practices throughout the continent. Two papers have been published recently based on these data. The first of these examined reactions occurring within 3 days of vaccination in 1.2 million dogs receiving 3.4 million doses of vaccine (some dogs receiving multiple doses during their puppy programme). The prevalence of any type of documented reaction was 38 dogs per 10,000 vaccinated – but it must be emphasized that the majority of these reactions were mild and of no clinical consequence. A parallel study examined reactions occurring within 30 days of vaccinating 496,000 cats with 1.2 million doses of vaccine. In this investigation the prevalence of adverse reactions was 51 per 10,000 cats vaccinated – but over half of these reactions were simply mild lethargy and fever following vaccination – an expected side effect related to immune stimulation. So adverse reactions based on these studies are **mostly mild** and are relatively uncommon, being in the **general order of 38 – 51 events per 10,000 vaccinations**. This study may have underestimated the number of immediate severe reactions because the animal would have been taken to an emergency clinic and it would not necessarily have returned to the Banfield Clinics. A general estimation of the prevalence of adverse reactions classified by severity would be:

- 0.2 – 1% (1 of every 100 to 500 vaccinations) for mild reactions

- 0.02 – 0.1% (1 in every 1,000 to 5,000 vaccinations) for moderate reactions
- 0.01 – 0.02 (1 in every 5,000 to 10,000) for severe reactions.

There is a wide **spectrum of adverse events** that have been associated with vaccination and these are summarized in Table 1. Many of these are **mild and transient** (1 – 2 days post-vaccination) reactions such as lethargy, low grade fever, soreness, stiffness, refusal to eat and sneezing/coughing after intranasal vaccination. **Moderate to severe** reactions include hives, facial oedema and anaphylaxis (where the animal, if not treated with adrenaline can die), feline injection site sarcoma (FISS) and autoimmune (autoallergic) diseases.

Table 1
Adverse Reactions Associated with Vaccination in Animals

Severe Reactions (Rare to Uncommon)	Moderate Reactions (Uncommon to Common)	Mild Reactions (Common)
Injection site sarcoma	Immunosuppression	Lethargy
Anaphylaxis	Behavioural changes	Hair Loss
Polyarthritis, hypertrophic osteodystrophy (HOD)	Vitiligo	Hair colour change at injection site
Immune-mediated haemolytic anaemia (IMHA)	Weight loss	Fever
Immune-mediated thrombocytopenia (IMTP)	Reduced milk production	Soreness
Glomerulonephritis	Lameness	Stiffness
Disease or enhanced disease the vaccine was designed to prevent	Granulomas/abscesses at the injection site	Refusal to eat (transient)
Myocarditis	Hives	Conjunctivitis
Post-vaccinal encephalitis or polyneuritis	Facial oedema	Sneezing
Seizures	Atopy	Coughing
Abortion, congenital anomalies, embryonic/fetal death, failure to conceive	Respiratory disease	Oral ulcers
	Allergic uveitis (blue eye)	Diarrhoea
	Skin disorders	Vomiting

It is generally only the adverse reactions that occur within the first few hours to a day after vaccination that are considered vaccine-associated by most veterinarians or owners. Even when the adverse reaction occurs shortly after vaccination there are many who fail to recognize that the vaccine caused the reaction. Certain adverse vaccine reactions are not observed until days, weeks or even months and years after vaccination or revaccination. The autoimmune disorders and the injection site sarcomas, which are among the rare vaccine adverse reactions, may not develop for years after being triggered by vaccines.

Because most adverse reactions are **genetically controlled**, certain dog **breeds** (especially some of the small breed dogs) and certain **families** of dogs and cats are more likely to develop adverse reactions than animals in the general population. That is why it is critically important for dog and cat breeders to record any adverse events believed to have occurred as a result of vaccination in their dogs and cats. When a given sire and bitch mating is known to produce pups that have a high percentage of adverse reactions to certain vaccines (e.g. facial oedema, anaphylaxis, seizures, atopic disease, haemolytic anaemia, encephalitis, arthritis), it would be desirable to neuter either or both of the parent animals, or be certain that the same two dogs are not mated again.

Certain of the small breed dogs have a greater likelihood of developing **immediate hypersensitivity reactions** (an immunological adverse reaction) after vaccination than do many of the large breed dogs. However, every breed has individuals that can develop such reactions post-vaccination. Certain vaccines are more likely to trigger these reactions than others. For example, the killed bacterial vaccines (bacterins) like *Leptospira*, *Bordetella*, *Borrelia* or the killed adjuvanted viral vaccines

like rabies virus vaccines are more likely to trigger an immediate hypersensitivity reaction than are the MLV vaccines; however, every type of vaccine can and does have the ability to trigger an immunological reaction in high risk animals. Breeders should carefully monitor the development of such reactions in the pups they sell and consider not breeding the same sire and bitch in the future. Some breeders of small breed dogs attempt to reduce the likelihood of adverse reactions by requesting that their veterinarian administer a split-dose of vaccine to their animals. The VGG strongly advises against this practice. Vaccines are formulated with a specific immunizing dose and unless the entire content of the vaccine vial is administered, the dog may fail to make a protective immune response.

Unfortunately, at times vaccines and vaccinations are often mistakenly blamed for causing or triggering various diseases and disorders when the vaccines are not responsible, and other factors (e.g. drugs, environmental contaminants, toxins, chemicals, infection or purely hereditary factors) are the cause of the problem. With many of the adverse reactions or disorders it is difficult or impossible to know if the vaccines and not something else caused the problem, because there are often multiple causes. As stated previously, under no circumstances should any breeder or owner NOT vaccinate their animal at least once at 16 weeks or older with the core vaccines because they are concerned about adverse reactions.

Adoption of the current vaccination guidelines as outlined above will minimize the risk of adverse reactions occurring in your pet following vaccination. Decisions made in consultation with your veterinarian related to core versus non-core products, frequency of administration based on extended duration of immunity products and avoidance of adjuvanted products (where possible) are all steps towards minimizing

risk. It must be stressed that simply not vaccinating is not an option – as the risks of contracting life-threatening infectious disease remains potentially high, even in developed countries.

Your veterinarian should discuss this **risk-benefit analysis** with you during a **consultation** that addresses the vaccination programme for your pet or breeding animals and offspring. You should be warned that any vaccination might induce a transient period of mild lethargy, inappetance and fever. Adverse effects related to vaccination will often occur within hours of administering vaccine, but some may take 2 – 4 weeks to be triggered, and FISS may take many months or years to become clinically apparent. Another type of adverse event is when a vaccine **fails to protect an animal from infection**. For example, if a fully vaccinated puppy contracts parvovirus infection, this should be regarded as a 'vaccine failure' and further investigated. In this instance the animal may be a non-responder or the last dose of vaccine may have been given at an age when MDA prevented immunity or alternatively, the vaccine may have been mishandled.

If you believe that vaccination has induced an adverse reaction then your first call should be to your veterinarian – particularly if the event requires further diagnosis or medical therapy. It is important that the suspected reaction is **recorded in your pet's health record**. The reaction should also be **notified to the manufacturer** of the vaccine and for this reason it is important that the specific details of the vaccines given (including batch numbers) are documented. This is now a requirement in some countries and such information must be entered onto the animal's **vaccination record card**.

Some countries also offer a means of reporting adverse reactions to a **government regulatory body** that will collect, analyse and periodically publish this information. Where such a scheme exists, it is also a requirement that the manufacturer reports adverse events made directly to them. Such programmes are however not widely available and many countries do not have them. Your veterinarian should generally make a report to the manufacturer or the regulatory reporting programme on your behalf, but in some instances it may be up to the pet owner to make such a report. Important details to have when making such reports include:

- Age, breed and sex of the animal
- Previous vaccination history
- Vaccines administered on this occasion (including components, manufacturers and batch numbers)
- Additional treatments, such as drugs or supplements, including nutriceuticals and holistic remedies
- Route of administration and site on the body of injection (if relevant)
- Nature of reaction
- Time after vaccination the reaction developed
- Whether further diagnosis or treatment was required or the reaction spontaneously resolved.

GLOSSARY

Abscess	A pus-filled lump often occurring under the skin.
Adaptive immunity	The body's reaction that tailors the immune response to specific disease agents (e.g. viruses, bacteria).

Adjuvant	A substance mixed with the microbial parts of a vaccine to enhance the immune response in a non-specific fashion.
Adverse event (following vaccination)	Any change in health or a 'side-effect' that occurs in an individual following administration of a vaccine.
Aerosol droplet	A suspension of fine particles or droplets in air.
Allele	Alternative nucleotide base sequences at the same physical locus in the DNA genome.
Anaemia	Decrease in the normal number of red blood cells or of the concentration of haemoglobin, the substance in blood cells responsible for oxygen transport.
Anaphylaxis	A severe, life-threatening allergic reaction.
Anorexia	Poor appetite that may lead to weight loss.
Antibody	Proteins (immunoglobulins) found in blood that are used by the immune system to identify and neutralize foreign objects, such as bacteria and viruses.
Antibody test	A means of demonstrating that an animal has been exposed to a particular infectious agent or vaccine by showing the presence of antibody to that agent in the blood of the animal. A positive antibody test indicates that the immune system of the animal has been exposed to a particular antigen and made a response to it.
Antigen	A substance recognized by the immune system that induces the synthesis of antibody and/or T-cells.
Antigen presenting cell	A cell that takes a complex antigen and converts it to a form whereby it can stimulate an immune response.
Antiserum	Blood serum containing antibodies; when injected, an antiserum passes on protection (passive immunity) to the recipient.

Arthritis	Inflammation of joints.
Attenuated organism	An organism that is still alive, but has lost the ability to cause disease or damage tissue. Organisms may be attenuated to include them in infectious vaccines.
Autoimmune (autoallergic) disease	Disease caused by an immune response to self antigen (e.g. autoimmune haemolytic anaemia, systemic lupus erythematosus).
Basic immunization programme	The series of vaccine injections given to pups/kittens plus the booster injection in the second year of life.
B lymphocyte	White blood cell responsible for production of antibody.
Blue eye	Cloudiness of the cornea (transparent front part of the eye that covers the iris, pupil and anterior eye chamber), as caused by adenoviruses in dogs.
Boosting	Reminding the immune system by presenting it an antigen it already knows; this may lead to an increase in antibody concentration and/or T-cell activity.
Broad-spectrum antibiotic	Has an activity against a wide range of disease-causing bacteria.
Canine respiratory disease complex	Colloquially known as 'kennel cough' in dogs. A disease of the upper respiratory tract of dogs resulting in chronic coughing – it is caused by a combination of factors including mixed infections with organisms such as canine parainfluenza virus, CAV-2, other viruses, *Bordetella*, other bacteria, *Mycoplasma*, environmental factors (e.g. dust, humidity) and stress.
Carrier (of virus)	An animal that harbors a virus without showing disease signs (inapparent carrier) and which can pass that virus on to other animals.
Cell-mediated immunity	Is performed by specialized (T) cells - the other immunity type is provided by antibody (humoral immunity).
Central nervous system	Brain and spinal cord.

Cerebellar ataxia	Erratic movement of a kitten due to damage of the cerebellum (the ‘little brain’ that controls movement) by parvovirus infection of queens during pregnancy.
Circulating immune complex	Antigen-antibody aggregates present in the blood stream that can stick in small blood vessels and cause disease.
Colostrum	Special milk produced by the mammary glands in early pregnancy, within one day of giving birth. Colostrum is rich in antibody and provides passive immune protection to newborn animals until they are capable of making their own immune responses.
Conjunctivitis	Inflammation of the mucous membranes of the eye.
Contagious	Infectious, communicable, transmissible, spreadable.
Core vaccine	Contains antigens of infectious agents every dog and cat should be protected against as those infectious agents cause lethal disease.
Corneal opacity	See ‘blue eye’.
Demyelination	Disease of the nervous system in which the insulating ‘myelin sheaths’ surrounding nerves is damaged or lost.
Depression	A reduction in the function of an organ, more generally: lack of energy.
Distemper myoclonus	Brief, involuntary twitching of a muscle or a group of muscles in the late phase of distemper.
DNA vaccine	A vaccine that does not contain an infectious agent, rather just a gene the codes for one part of that agent that can trigger a strong immune response.
Duration of immunity	Time span of immune protection, e.g. after infection or vaccination.
Encephalitis	Inflammation of the brain.

Encephalomyelitis	Inflammation of the brain and spinal cord.
Enteric infection	Infection of the gut. May cause vomiting and diarrhoea.
Evolution (virus)	The combination of mutation and selection of viruses, leading to disease agents with novel (or changed) properties. Influenza viruses are excellent examples.
Feline injection site sarcoma	Malignant tumour developing in cats at places where injections may have caused chronic inflammation – often months or years previously.
Feline respiratory disease complex	Disease of the upper respiratory tract caused by a combination of underlying factors (e.g. environmental factors [dust, humidity], stress) and a number of infectious agents including FCV, FHV-1, bacteria and *Mycoplasma*.
Fomite	Any inanimate object or substance capable of carrying infectious organisms (such as germs or parasites) and hence transferring them from one individual to another.
Gene	The unit of heredity in a living organism, a stretch of DNA that codes for a protein.
Glomerulonephritis	Inflammation in one part of the kidney.
Granuloma	A collection of inflammatory cells. Small granulomas may form at the site of vaccination, particularly where adjuvanted vaccines are injected.
Half life (of antibody)	The time taken for one half of the mother's antibody taken up from colostrum, and present in the blood of a newborn animal, to degrade and disappear. A half life of 10 days indicates that if an animal has 100 units of antibody in the blood, 10 days later there will be only 50 units remaining.
Hard pad disease	A specific form of distemper characterized by thick crusting of the pads of the feet (hyperkeratosis).

Herd (population) immunity	Occurs when the vaccination of a portion of the population (or herd) provides protection to unprotected individuals. It is difficult for an infection to establish where more than 75% of a population is vaccinated.
Humoral immunity	Immunity conferred by antibodies.
Hyperkeratosis	Thickening of the superficial layer of the skin; often associated with a qualitative abnormality of the keratin.
Immediate hypersensitivity	An allergic reaction that occurs within minutes to hours of exposure to a trigger.
Immune-mediated disease	A disease caused by an abnormal immune response. Includes autoimmune and hypersensitivity-mediated diseases.
Immune-mediated haemolytic anaemia	Anaemia caused by the immune system inappropriately attacking and destroying the red blood cells (an example of autoimmune disease).
Immune-mediated thrombocytopenia	A bleeding disease due to lack of platelets in the blood. The platelets are inappropriately destroyed by the immune system.
Immunization	Induction of a protective immune response after natural infection or after administration of a vaccine.
Immunological memory	Throughout the lifetime of an animal specialized 'memory' white blood cells will 'remember' each specific pathogen encountered, and are able to mount a strong and quick response if the disease agent is detected again. This type of immunity is both active and adaptive because the body's immune system prepares itself for future challenges.
Immunosuppression/immunodeficiency	Reduction or absence of the activation or efficacy of the immune system. May be caused by a range of different factors including genetics, infection, drugs (medical immunosuppression) or chronic disease such as cancer.
Inactivated organism	A killed or dead organism found in non-infectious vaccines.

Incubation period	The time between exposure to a pathogenic organism and when disease signs are first apparent.
Infectivity	Infectious property.
Infection pressure	The continuous infection risk in an environment with a high load of infectious agents (e.g. in an animal shelter).
Infectious canine laryngotracheitis	Synonym for 'kennel cough'. See also Canine Respiratory Disease Complex.
Infectious vaccine	A vaccine containing a modified live or attenuated infectious agent. Also includes viral vectored recombinant vaccines (e.g. rCDV). These are the most effective type of vaccines. See modified live vaccines.
Inappetence	Lack of appetite.
Innate immunity	Protection by cells and mechanisms that immediately defend the host from infection in a non-specific manner. Cells of the innate system recognize and respond to pathogens in a generic way and do not confer long-lasting immunity.
Interferons	Proteins made and released by cells in response to the presence of pathogens (e.g. viruses, bacteria, or parasites) or tumor cells. They allow communication between cells to trigger the protective defenses of the immune system that eradicate pathogens or tumors.
Intramuscular	Injection of a vaccine into the muscle.
Intranasal	Administration of a vaccine into the nose through the nostril.
Jaundice (icterus)	Yellow discoloration of skin and mucosal membranes. Generally indicates either liver disease or a specific type of anaemia.

Kennel cough	Infectious canine laryngotracheitis; also referred to as canine respiratory disease complex (CRDC).
Keratitis	Inflammation of the cornea, the transparent front part of the eye that covers the iris, pupil and anterior eye chamber.
Killed (non-infectious) vaccine	Contains dead infectious agents or selected antigens (proteins, polysaccharides) of infectious agents, but no live, replication-competent viruses, bacteria etc. These vaccines contrast to those produced by attenuating the virus (modified live vaccine). Also termed 'non-infectious vaccine'.
Latent infection, latent virus	Subclinical infection, without noticeable disease signs. Viral latency is a form of dormancy in which the virus does not replicate. Primarily seen with herpes viruses and retroviruses.
Leucocytes	Collective term for white blood cells of the immune system defending the body against infectious agents, cancer cells and anything foreign invading the body.
Life-long protection	Immune protection afforded by some viral infections and vaccinations.
Live attenuated vaccines	Synonym: infectious vaccine or modified live vaccine. They are developed by reducing the disease-causing properties of a pathogen, but still keeping it viable (or 'live'). Attenuation takes a living agent and alters it so that it becomes harmless or less virulent. These vaccines contrast to those produced by killing the disease agent (inactivated vaccine).
Lymphocyte	Specialized types of white blood cells of the immune system defending the body against infectious agents, cancer cells and anything foreign invading the body.
Lymph nodes	Organs of the immune system, distributed widely throughout the body and linked by lymphatic vessels; found all through the body, and acting as filters or traps for foreign particles. They are important in the proper functioning of the immune system and in generating the immune response to a vaccine.
Lymphoid depletion	Exhaustion or reduction of cells of the lymphoid system.

Lymphoid tissue	Tissue associated with the lymphoid system and concerned with immune functions in defending the body against infections and spread of tumours. It consists of connective tissue with various types of white blood cells enmeshed in it, most numerous being the lymphocytes.
Lymphopenia	Lack of lymphocytes in the blood.
Maternally-derived antibody	Antibodies taken up by pups or kittens through the intestinal tract from the dam's colostrum and milk during the first few days after birth.
Modified live vaccines	Synonyms: Live attenuated vaccine or infectious vaccine. They are developed by reducing the disease-causing properties of a pathogen, but still keeping it viable (or 'live'). Attenuation takes a living agent and alters it so that it becomes harmless or less virulent. These vaccines must infect the animal to immunize. These vaccines contrast to those produced by killing the disease agent (inactivated vaccine).
Morbidity	Disease or illness. The rate of disease in a population.
Mortality	Death following disease. The rate of death in a population following disease.
Mortality rate	A measure of the number of deaths in a given population following disease.
Mutation (virus)	Changes in the nucleotide sequence (the genetic information) of a viral genome caused by e.g. radiation or chemicals, as well as errors that occur during replication. The mutation may or may not lead to antigenic changes in the organism.
Myocarditis	Inflammation of the wall of the heart.
Natural killer (NK) cell	A type of cytotoxic lymphocyte and a major component of the innate immune system; they play a major role in the rejection of tumours and virus-infected cells.
Neutropenia	Lack of neutrophil granulocytes (a specialized type of white blood cell) in the blood.

Non-core vaccines	Are to protect against infectious agents that not every dog or cat risks being exposed to. Their use should be carefully considered and they should only be given to animals with a defined exposure risk.
Non-infectious vaccine	See killed vaccine.
Not-recommended vaccines	Licensed products without an indication; products intended to protect against mild, self-limiting, treatable disease; or vaccines of doubtful efficacy.
Non-responder (to vaccination)	An animal that fails to mount a protective immune response (antibody) following vaccination. This is often breed-related in dogs and likely to be genetically determined.
Oedema	Abnormal accumulation of fluid beneath the skin or in one or more cavities of the body.
Oral ulcer	Open sore inside the mouth.
Oronasal infection	Infection of the mouth and nose.
Panleukopenia	Literally: loss of all types of white blood cells; in the cat a disease caused by a parvovirus infection.
Pathogen	Disease-causing agent (e.g. prion, virus, bacterium, parasite).
Pneumonia	Inflammation of the lungs.
Polyarthritis	Inflammation of multiple joints.
Polymerase chain reaction (PCR)	A means of detecting the presence of a microbial agent in an animal by demonstrating the presence of the genetic material (DNA or RNA) of that agent in a sample (e.g. of blood). A positive PCR test does not indicate that the agent is alive.
Polyneuritis	Inflammation of multiple nerves.
Potency of a vaccine	A measure of the activity of a vaccine in a host.

Priming	The first stage of a process occurring when an antigen is presented to lymphocytes causing them to differentiate into effector cells and into memory cells. The first dose of a non-infectious vaccine generally primes the immune response and a second dose is required to immunize. In contrast, the first dose of an infectious vaccine will prime and immunize and even boost the immune response because new antigen is produced as a result of infection. That is why one dose of an infectious vaccine will immunize, whereas two doses of a non-infectious vaccine are required to be given 2 – 6 weeks apart to immunize and subsequent doses should boost.
Quarantine	Compulsory isolation to contain the spread of an infectious disease.
Reactivation (of virus)	Terminating latency of a virus and making it replicate and shed (like in feline herpesviruses).
Replication (virus)	Multiplication in a cell.
Resistant (virus)	Virus that no longer responds to antiviral treatment or a virus that resists environmental decontamination and can remain present and capable of causing infection in a susceptible host.
Revaccination interval	Time period between revaccinations.
Rhinitis	Inflammation of the nose.
Risk-benefit analysis	Comparison of the risk of a situation to its related benefits.
Secondary infection	Primary and secondary infection may either refer to succeeding infections (first viral, followed by bacterial), or to different stages of one and the same infection.
Serotype (virus)	A serotype is a group of viruses classified together based on their antigens. It also distinguishes serological differences among viruses, which may be important in vaccine protection (e.g. serotype A may or may not protect against serotype B).
Shedding (of virus)	Virus released from an infected organism into the environment.

Spleen	Organ found in vertebrates with important roles in regard to red blood cell storage and production and the immune system.
Sterile immunity	A potent immune response that completely clears an infection or makes the animal able to resist infection. Only a few vaccines induce sterile immunity, but this is the ultimate form of vaccine protection.
Subclinical infection	Infection without disease signs.
Subcutaneous	Injection of a vaccine beneath the skin into the underlying (subcutaneous) tissues.
T lymphocytes	A group of white blood cells that play a central role in cell-mediated immunity; the abbreviation T stands for thymus, since this is the principal organ responsible for the production of mature forms of these cells.
Thrombocytopenia	Lack of platelets (small cells in part responsible for clotting) in the blood.
Tonsil	Lymphoid tissue in the mouth.
Vaccination	The act of administering a vaccine. Vaccination does not necessarily mean that the animal has been immunized. For example, in young animals, multiple vaccines must be administered to ensure that one dose is not blocked by MDA.
Vaccine-induced antibody	Antibody found after vaccination.
Vestibular disease	Disease affecting the vestibular system, which is responsible for body balance and spatial orientation, movement and equilibrium.
Viraemia	Virus circulating in the bloodstream.
Virulence	Disease-causing potency of an organism.
Virulence variant	A mutant of a disease agent, whose disease-causing potency is higher or lower than that of the parent agent.