Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Review

Review of companion animal viral diseases and immunoprophylaxis

J.R. Patel\textsuperscript{a,\ast}, J.G.M. Heldens\textsuperscript{b}

\textsuperscript{a}JAS Biologicals Limited, The Centre for Veterinary Science, Madingley Road, Cambridge CB3 0ES, UK
\textsuperscript{b}Intervet Schering-Plough Animal Health, W. de Köverstraat 35, 5830 AH Boxmeer, The Netherlands

\textbf{ARTICLE INFO}

Article history:
Received 11 August 2008
Accepted 5 November 2008
Available online 27 November 2008

Keywords:
Veterinary viruses
Viral vaccines
Viral diseases
Epidemiology
Pathogenesis
Companion animals

\textbf{ABSTRACT}

In this article we review important established, newly emergent and potential viral diseases of cats, dogs and rabbits. Topics covered include virus epidemiology, disease pathogenesis, existing and prospective immunoprophylaxis against the viruses. For some feline viruses, notably the immunodeficiency virus, leukaemia virus and peritonitis virus, available vaccines are poorly efficacious but there are good prospects for this. A further challenge for the industry is likely to be due to viruses jumping species and the emergence of more virulent variants of established viruses resulting from mutations as has been the case for the canine parvovirus, coronaviruses and feline calicivirus.

© 2008 Elsevier Ltd. All rights reserved.

\textbf{Contents}

1. Introduction ................................................................. 491
2. DNA viruses ................................................................. 492
  2.1. Herpesviridae ......................................................... 492
  2.2. Adenoviridae ......................................................... 492
  2.3. Poxviridae ............................................................... 492
  2.4. Parvoviridae ............................................................ 493
3. RNA viruses ................................................................. 493
  3.1. Caliciviridae ............................................................ 493
  3.2. Coronaviridae ........................................................ 494
  3.3. Paramyxoviridae ..................................................... 495
  3.4. Rhabdoviridae ......................................................... 495
  3.5. Retroviridae ............................................................ 495
4. Emergent and potential virus diseases ............................................. 496
5. Immunoprophylaxis ......................................................... 500
6. Conclusions ................................................................. 501
Acknowledgements ........................................................... 501
References ............................................................. 501

1. \textbf{Introduction}

Viruses of many families cause disease in small companion animals and there is much academic and industrial interest in understanding disease pathogenesis, virus transmission in the field and prophylactic control of diseases. Companion animal viral vaccines represent a significant share of the global veterinary vaccines market to which several manufacturers offer products. Most products, however, are formulated using old vaccine viral strains which in some instances, are in need of updating in view of emergence of more virulent strains in the field. Pathogenic mutants with altered organ tropism have for instance emerged in case of carnivore par-
Adenoviruses were first named in 1956 to cluster a new group of cytopathic viruses recovered from explanted human adenoid and tonsillar tissue. The family has two genera, the mastaadenoviruses from mammals and aviaadenoviruses from birds. Genera are further classified into subgenus, species and strains. Adenoviruses cause disease in dogs and pigeons. Two antigenically related adenoviruses species can cause significant disease in domestic dogs and other canids. The two viruses involved are commonly known as canine adenovirus-1 (CAV-1) and 2 (CAV-2) and also as infectious canine hepatitis virus and infectious canine laryngotracheitis virus respectively. The close antigenic cross-reactivity is seen at the level of significant reciprocal but unequal cross-neutralisation. The viruses are however unequivocally distinguished by DNA fingerprinting of endonucleases digests of viral DNA. CAV-1 occurs worldwide and infects and replicates in oropharynx after the ingestion of infectious material from respiratory secretions, urine or faeces. The primary replication in tonsils, Peyer's patches and epithelia of oropharynx and bowel results in lymphoid cell viraemia which initiates secondary infection of parenchyma of liver, kidney and lining of blood vessel and sinusoids in these organs and other sites. Infected cells die and lyse leading to main pinpoint bleeds and haemorrhages and some times a large bleed if a major vessel is involved. CAV-1 causes fatal hepatitis in newly weaned puppies and susceptible young dogs. Other lesions due to CAV-1 infection comprise subcutaneous oedema, ascites and oedema of the gall bladder wall, immune complex keratitis and nephritis. Older dogs may be susceptible but signs are milder with enlargement of tonsils, sub-maxillary lymph nodes and sometimes immune complex keratitis. Isolates of CAV-1 vary in virulence for the domestic dog, some cause sub-clinical diseases while others acute disease with severe abdominal pain followed by death. Wild and farmed dogs are highly susceptible to some strains of CAV-1 encephalitis. CAV-1 can often cause immune complex vasculitis, commonly known as blue eye.

CAV-2 transmission among dogs is mainly by inhalation and virus is widely prevalent. CAV-2 is a major cause of kennel cough syndrome. CAV-2 causes extensive lesions in the upper and the lower respiratory tract resulting in interstitial pneumonia often with necrotising bronchitis and bronchiolitis, focal necrosis of the turbinate and tonsillar epithelium. The disease is more severe when associated with concurrent bacterial infection. Often the bronchial nodes are congested and haemorrhagic but gross liver and gall bladder lesions are usually absent. CAV-2 infection in dogs has not been associated with hepatitis. Other signs of CAV-2 infection may be fever, mild depression and nasal and/or ocular discharge; corneal opacity is sometimes seen.

2.3. Poxviridae

Members are large, enveloped, highly resistant viruses with a double-stranded linear DNA genome which replicates in cytoplasm of infected cells. The subfamily Chordopoxvirinae has members affecting vertebrates classified into six genera [10]. The vertebrate poxviruses usually produce proliferative focal lesions and are occasionally fatal when they generalise. Members are very stable and virus shed in scabs survives for months or years in dust particularly in dry conditions. Companion animal species affected by poxviruses are rabbits, pigeons and mild disease due to cowpoxvirus has been reported in cats. Myxomavirus (MV) in genus leporipoxivirus causes myxomatosis, a systemic and usually a fatal disease in European rabbits (Oryctolagus cuniculus) but a benign disease in its natural host, Sylvilagus rabbits in the Americas [11,12]. MV spreads mechanically by blood-feeding arthropod vectors such as mosquitoes and fleas and to a lesser degree by direct contact.
or aerosol [9]. Virus remains infectious for several months in vectors. In rabbit MV replicates subcutaneously locally followed by viraemia and generalised dissemination to connective tissue cells initiating a proliferative response and exudative erythematous dermatitis around the face, eyes and skin surfaces generally. The lesions become ulcerated and covered with weeping crusts [11,12]. Field epizootics have resulted in mortality rates approaching 100%.

Cats occasionally become infected with a poxvirus which is indistinguishable from cow poxvirus in genus orthopoxvirus. Infection in cats is acquired from rodent bites and develops as small red macular eruptions which develop into papules or ulcers which scab over several days on the legs and/or head which in some infected cats become more widespread and may spread to lungs.

2.4. Paroviridae

Members are the smallest, along with circoviruses, of DNA viruses and include important pathogens of cats and dogs. Paroviruses and circoviruses have a predilection for replication in rapidly dividing cells of bone marrow, enteric epithelium and the foetus. A parovirus with predilection for rabbit small intestine and lymphoid tissues and liver has been known for sometime but the virus does not appear to be a significant rabbit pathogen and only causes mild catarrhal enteritis [13]. Members have an icosahedral capsid with an over all diameter of 18–25 nm and contain linear, single-stranded DNA.

The known carnivore paroviruses named feline panleukopenia virus (FPLV), canine parovirus (CPV-types 1, 2, 2a, 2b and 2c), mink enteritis virus (MEV-types 1, 2 and 3) and those isolated from wild felids and canids such as raccoons, foxes (red and blue species), leopards and cheetahs are genetically related and interspecies transmissions among carnivores occur readily [14,15]. CPV-2 was first recognised in 1978 as the cause of new disease in dogs which rapidly spread worldwide [16–19]. Evidence suggests that the CPV arose from the long recognised FPLV or related virus infecting another carnivore such as mink, raccoon, artic fox or other. The new virus differed from FPLV like viruses in less than 1% in genomic sequence [20–23]. However, the life of firstly identified CPV variant in nature was brief [24]. By 1981 CPV-2 was replaced by CPV-2a which in turn was replaced between 1984 and 1990 by CPV-2b. In each case the replacement was global. Interestingly, CPV-2 and its 2a and 2b variants differed by less than 0.2% in their genome sequence and involved substitution of 3–4 amino acids in virus capsid protein VP2 [20–23,25]. This change was ongoing with the identification of CPV-2c in late 1990s [26]. The latter variant has also spread widely [27]. CPV-2c has one amino acid substitution in VP2 [26]. Whilst this change in VP2 is minor it was nonetheless significant in conferring a broader host range phenotype to the variants. Thus experimentally cats were refractory to infection by CPV-2 but readily susceptible to infection by CPV-2a and 2b viruses [23]. These viruses occur worldwide and are evolving rapidly [28,15,29]. However, their evolutionary history is complex and possibly not fully unravelled and it has been suggested that their current classification and naming of new isolates needs revision [15].

A key factor in the epidemiology and evolution of carnivore paroviruses has been the virus tropism for the gut and the survival of virus shed in faeces for long periods (several months to 2 years). Faecal-oral route is the main mode of virus transmission of these important carnivore viruses. However, in vivo tissue tropism of FPLV and CPV vary with respect to ability to replicate in enteric epithelium and produce faecal virus in quantity. In cats FPLV replicates in lymph nodes, thymus, spleen and intestine and large quantities are shed in faeces while in dogs FPLV replication occurs in the thymus and bone marrow but not in the gut and mesenteric lymph node [30]. CPV and FPLV also initiate infection in the mucosa and lymphoid tissue of the buccal cavity and result in leukocyte-associated viraemia followed by progeny virus spread to internal organs. In puppies ingested virus replicates in crypts of small intestine resulting in leukocyte viraemia, viral dissemination and secondary infection of the liver and of cardiac myocytes although the latter is rarely seen today due to effective vaccination. Infection of these vital organs may cause eventual heart failure associated with pulmonary oedema, hepatomegaly and ascites. Mortality is high. In older dogs ingested virus replicates in intestinal crypts which more commonly results in vomiting, diarrhea and leucopoenia with high morbidity but low mortality.

Pathogenesis of FPLV infection in cats is similar to CPV disease in dogs. Viraemia following the respiratory and the enteric phases of viral replication leads to secondary infection of bone marrow, spleen and lymph nodes. This results in transient leukocytosis followed by a marked leucopoenia and anaemia. Virus is shed by most routes 2–6 days after infection.

3. RNA viruses

3.1. Caliciviridae

Members are non-enveloped icosahedral very small (27–40 nm) viruses with a linear, positive sense single stranded RNA genome and replicate in cell cytoplasm. Three viral species in family Caliciviridae cause significant diseases in cats, rabbits and brown hares. Feline calicivirus (FCV) belongs to the distinct phylogenetic clade in genus vesivirus. Rabbit haemorrhagic disease virus (RHDV) and European brown hare syndrome virus (EHHSV) belong to the distinct phylogenetic clade in genus lagovirus. RHDV and EBHSV share antigenic epitopes which elicit cross-protective antibodies. Caliciviruses are not considered significant pathogens of domestic dogs nor are they isolated frequently. However both FCV related and unrelated caliciviruses have been isolated from faeces of puppies and dogs with diarrhea [31–33]. Canine caliciviruses (CCoV) at present remain unclassified [34]. However, it is possible that one or more of these dog isolates of caliciviruses have the potential to adapt, spread and establish in dog populations to cause clinically important disease. Caliciviruses do mutate readily in nature as is indicated by the emergence of a highly virulent haemorrhagic variant of FCV [35–37] which has spread rapidly [38,39]. The newly emerging FCV variants have been named virulent systemic FCV (VS-FCV) to distinguish them from the common FCV strains. FCV has a worldwide distribution while VS-FCV is, at present, limited to USA and the UK [36] but very likely to become more prevalent. VS-FCV strains appear to have arisen independently of one another and have not spread from a single case [37]. Both virus types are excreted in urine, saliva, ocular and respiratory secretions and are transmitted via aerosol, oral and on fomites. Usually, virus shedding is for up to 2 weeks but some recovered cats shed the virus intermittently [40]. Primary infection by both virus types is often in the upper respiratory tract and/or oral mucosa with an incubation period of 2–3 days resulting in epithelial cell necrosis with vesicle or ulceration of the external nares and oral mucosa. Virulent FCV strains may also cause interstitial pneumonia. Infected cats may also manifest fever, anorexia, conjunctivitis, lethargy and stiffness, nasal and ocular discharge, sneezing and rales. Some FCV but most VS-FCV strains are fatal [35,36].

RHDV and EBHSV infections are highly contagious and acute fatal diseases caused by distinct but antigenically related caliciviruses. RHD was first reported in the People’s Republic of China in imported Angora rabbits imported from German Democratic Republic [41] while EBHS was described in brown hares (Lepus europaeus) and mountain hares (Lepus timidus) in 1981 in Sweden [42]. However, epidemiological investigations indicated presence
of these viruses in Europe much before the above published reports. One line of data supporting this conclusion was the detection of RHDV antibodies in rabbit sera collected in early 1970s [43]. RHDV is endemic in most parts of Europe, Asia and parts of Africa, Australia and New Zealand. RHDV was imported into Australia in 1991 for biological control of wild rabbits but the virus escaped from Wardang island quarantine facility in 1995 and became established across Southern Australia [44]. Insect vectors were suspected as to have spread the virus from Wardang Island [45]. EBHSV is widespread wherever hares (L. europaeus and sub species) are endemic as is the case in Europe [46]. Rabbit species vary in their susceptibility to RHDV infection. American cottontail rabbits (Sylvilagus floridanus) appear to be refractory to infection by RHDV [47,48]. RHDV transmission is by direct contact and via fomites [45]. Thus primary infection is at an oral and/or conjunctival mucosa. EBHSV is likely to be similarly transmitted among hares. Flies of the genus Phorbia in Europe transmit RHDV via the conjunctiva while in Australia bush flies (Musa vestustissima) and blow flies (Caliphora dubia) were identified as potential vectors [49,50,45]. Rabbit fleas (Siphonophorus cuniculi and Xenopsylla cunicularis) and mosquitoes (Culex annulirostris) were shown to transmit RHDV to rabbits under laboratory conditions [51,45]. Molecular epidemiological studies, thus far, have shown a low (less than 10% nucleotide) genomic variation among RHDV isolates collected over a period of several years from different geographical areas [52,53]. However, natural mutational changes in the field have been recorded [54]. A question that remains unresolved is that of how virus persists in nature from year to year. Typically in the field RHDV infected rabbits die within 24–48 h with few outward signs excepting bloody mucous discharge from the nose.

Following the primary replication in oronasal and/or ocular mucosa RHDV infects macrophages and other mononuclear cells (circulatory and alveolar macrophages) and these infected cells disseminate the virus to the internal organs particularly the liver and kidneys where virus undergoes secondary replication [55]. Cells of the mononuclear phagocyte lineage are also likely to be involved in transmission of EBHSV to the internal organs of infected hares. In both RHD and EBHS, a consistent finding is severe necrotising hepatitis, characteristic lesion being coagulation liver necrosis in RHD and lytic necrosis in EBHS [56]. However, the two diseases also have characteristic pathological differences. In RHD, disseminated intravascular coagulation (DIC) and thrombini in kidneys and lungs are common lesions while DIC has not been observed in hares with EBHS and haemorrhages are also infrequent [56]. Depletion of splenic lymphocytes is observed in both diseases. Apoptosis of hepatocytes, macrophages and endothelial cells along with DIC and progressive jaundice are common features in RHD of rabbits [57]. An interesting hypothesis put forward to explain the differences in types of lesions between RHD and EBHS was suggested as due to the genetic difference between the two affected lagoon species. Evidence supporting this hypothesis has been the observation of liver lesions in RHDV infected hares that were indistinguishable from those seen following EBHSV disease of hares [56]. Thus the type of lesions is apparently not determined by the virus species. As in FCV infection of cats, protection against RHDV disease is conferred by virus neutralising antibody to the major viral capsid protein namely VP60 in RHDV.

### 3.2. Coronaviridae

Coronaviruses (CoVs) (family Coronaviridae, order Nidovirales) are a group of enveloped positive-strand large RNA viruses of mammals and birds and are found worldwide. The coronavirus genus has been classified into three clusters or groups based on antigenic cross reactivity and other criteria. Group 1 has dog (CCoV), cat (FCoV), human (HCoV-229E), pig epidemic diarrhoea (PEDV), pig respiratory (PRCoV), pig transmissible gastroenteritis (TGEV) CoVs. Group 2 species are bovine (BCoV), human (HCoV-OC43), mouse (MHV), pig haemagglutinating encephalomyelitis (HEV), SARS (SARS-CoV), canine respiratory coronavirus (CRCoV) and other CoVs. Group 3 consists exclusively of avian CoVs. Most members usually cause mild enteric and/or respiratory disease and hence are generally considered of minor clinical importance. There are however exceptions (see below). The large genome is prone to high frequency mutations [58–60]. CoVs have the potential to jump the species barrier and cause severe disease as was the case for severe acute respiratory syndrome (SARS) in Southern China [61]. Studies by different groups demonstrated that SARS-CoV succeeded in spillover from a wildlife reservoir (probably bats) to human population via an intermediated host(s) and that rapid viral evolution played a key role in the adaptation of SARS-CoVs in at least two non-reservoir species within a short period [62]. It has been shown that cats and ferrets can be infected with this virus as well [63]. Virus transmission is by inhalation and/or ingestion of virus in faeces, saliva and aerosol. This results in limited virus replication in upper respiratory tract (URT) and/or intestinal mucosa and associated lymphoid tissues and progeny virus does not normally or only limitedly generalises to internal organs with some exceptions. However combined secondary bacterial infection often exacerbates the clinical disease. Dogs are susceptible to two CoVs, the enteric (CCoV) [64] and the newly recognised respiratory CoV (CRCoV) [65,66]; the latter virus has been placed in antigenic group 2 along with BCoV and others. The group 1 CoVs have been placed into two serotypes (I and II). CCoVs primarily cause mild enteric disease in puppies manifest as fever, depression, anorexia and diarrhea. Severe disease due to CCoV is infrequent [60]. However, a pantropic virulent variant of serotype II CCoV with much broader viscerotropic phenotype was recognised recently [67]. This variant (designated CB/05), in addition to the usual enteric replication, also spreads to and replicates in internal organs (lungs, spleen, liver, kidney and brain) and was the cause of deaths of some dogs [67–69].

FCoVs occur as two serotypes with different serological and biological characteristics, particularly in sequence homology of the viral surface S glycoprotein [59]. Like CCoVs, most FCoVs cause mild enteric disease but could give rise to highly pathogenic variants in individual infections causing peritonitis (FIP). Both serotypes of FCoV mutate to virulent FIPV variants. Their relative prevalence in nature varies but type I FIPV/FCoV strains are generally dominant in the field [70]. FIPV variants of FCoV have been the cause of fatal peritonitis in some cases [71,72]. FCoVs are transmitted via the faecal-oral route and primarily replicate in enterocytes [73] from where the progeny virus disseminates to internal organs via monocyte-associated viraeemia. Although FCoV is highly prevalent, FIP morbidity is relatively low, rarely exceeding 5% [73]. Feline infectious peritonitis (FIP) is a progressive debilitating disease. A pathognomonic feature of FIP is widespread occurrence of pyogranulomatous lesions in majority of organs (lungs, liver, spleen, omentum and brain) and other tissues [74,75]. Other features of FIP involve a marked T-cell depletion, particularly in end-stage FIP [76] and hyperggammaglobulinemia [77]; B-cell leucopenia is also a feature in FIP disease [78]. The T-cell depletion is apparently not the result of virus infection since T-cells appear not to support virus replication [76]. Other important determinants in FIP pathogenesis appear to be (i) dissemination of mutant progeny FIPV by activated macrophages and monocytes and their availability [79] and (ii) types of viral S protein neutralising antibodies at suboptimal concentration which opsonise the virus and enhance its infectivity for target cells via Fc receptor mediated attachment [80–82]. There is also complement activation with resultant platelet aggregation, intravascular coagulation necrotising lesions and exudation of fluid
into the abdomen and thoracic cavity in the so-called wet form of FIP. Wet FIP is most common in kittens under one year of age and the incidence declines by 5 years of age when the dry form of FIP is more common [82]. Whilst there is no protective immunity in wet FIP, the dry form is a result of partial immunological protection [82–83]. Some of these pathogenetic features of FIP notably the T-cell lymphopenia, multiphasic disease course and viral persistence have been seen in SARS. Both these diseases are an enigma possibly stemming from virus-induced immune dysregulation.

3.3. Paramyxoviridae

Members in the family are enveloped viruses with single stranded negative-sense RNA genome. Currently the family Paramyxoviridae has two subfamilies named Paramyxovirinae and Pneumovirinae. The former has five genera: respirivirus, morbillivirus, rubulavirus, henipavirus and avulavirus. The latter has two genera: pneumovirus and metapneumovirus. The members survive moderately well in the environment; all replicate in the upper respiratory tract epithelium and have a broad host range affecting farm and companion animals, birds and man. Some members also have cell tropism for reticuloendothelial, enteric and neural cells causing significant pathology and disease of the bowel and/or CNS. In dogs two members are significant pathogens. The viruses concerned are canine distemper virus (CDV) in genus morbillivirus and parainfluenza virus-2 (PIV-2) in genus pneumovirus. Both viruses are transmitted by aerosol which initiates primary infection in respiratory tract and/or tonsilar epithelium and dissemination throughout the bronchial tree. Two-5 days later respiratory disease may follow with signs of primary fever, dyspnoea, nasal discharge, inappetance.

Progeny virus from primary CDV replication also initiates infection of macrophages and then of lymphocytes both of which disseminate the progeny virus to the epithelium and lymphoid tissue of small intestine giving rise to vomiting and diarrhoea and then anaerxia. Other organs infected following macrophage-lymphocyte viraemia are neurones and brain macrophages and epithelia of endometrium. Significant infection at these sites may result in CNS disease and/or transplacental invasion of the foetus which may die. The CNS disease signs observed are ataxia, muscle tremors and paralysis and coma. PIV-2 has been associated with kennel die. The CNS disease signs observed are ataxia, muscle tremors and coma. FIP. Wet FIP is most common in kittens under one year of age and the incidence declines by 5 years of age when the dry form of FIP is more common [82]. Whilst there is no protective immunity in wet FIP, the dry form is a result of partial immunological protection [82–83]. Some of these pathogenetic features of FIP notably the T-cell lymphopenia, multiphasic disease course and viral persistence have been seen in SARS. Both these diseases are an enigma possibly stemming from virus-induced immune dysregulation.

3.4. Rhabdoviridae

Rabies virus (RV) in genus lyssavirus of family Rhabdoviridae has long been the most feared zoonosis. All mammals are susceptible to RV. Viral particles are bacilliform and/or bullet-shaped, enveloped and contain one molecule of non-infectious, linear, negative-sense, single-stranded RNA. Common reservoir hosts are members of canids (fox, dog, wolf and jackal), mustelidae (skunk, polecat and some other species) and chiroptera (bats). RV transmission is usually by bite of infected animals shedding virus produced in salivary gland. Primary virus replication occurs in muscle fibres at the site of bite from where the progeny virus gains access into the nerve fibres and migrates along the axoplasm centripetally. Once in the neurone cell body virus replicates followed by centrifugal migration down the cranial nerves to the salivary gland where the virus replicates and is shed in saliva. RV occurs worldwide with the exception of countries which practice strict quarantine regulations. Rabies is an increasing threat to cats and dogs in endemic areas and the infection is almost always fatal after a paralytic and respiratory distress disease. In usual circumstances the only risk of rabies virus transmission is by the bite or scratch of a rabid animal, highly humid environment such as in bat caves the virus may be transmitted via aerosols as well. The control of rabies in different regions of the world poses very different problems, depending on which reservoir hosts are present and the level of infection therein [9].

3.5. Retroviridae

The family name derives from members possessing reverse transcriptase enzyme (RT). The family is sub divided into 3 subfamilies: Oncovirinae, Lentivirinae and Spumavirinae. Members in the subfamily are further classified as genera, subgenera and species. Virus particles are enveloped covering anicosahedral capsid containing helical nucleocapsid. The genome comprises two copies of linear positive-sense, single-stranded RNA (+ssRNA) which is not infectious per se. The viral genome occurs as an inverted dimer held together at the 5’ end by hydrogen bonds possibly through base pairing. Retrovirus replication is unique among +ssRNA viruses because they first convert +ssRNA to –DNA copy using the virion RT (RNA dependent DNA polymerase) and then a circular double-stranded (DS) DNA copy which is integrated into host cell chromosome by a second viral enzyme, a DNA ligase. The integrated DS DNA then codes for new +ssRNAs which then serve as new genomes or messenger RNAs. The latter stage of viral replication is catalysed using cellular enzymes and organelles.

In companion animals Feline leukemia virus (FeLV) in subfamily Oncovirinae and feline immunodeficiency virus (FIV) in subfamily Lentivirinae cause significant diseases in cats. However in dogs and rabbits retroviruses are not significant pathogens. FeLV is a leading killer of cats causing lymphosarcoma and leukaemia which are the most important and common tumours of cats. Cats become infected through close contact with other infected cats and ingestion of or contamination from licking of wounds by infectious saliva during mutual grooming. Virus replicates in oropharynx and/or leukocytes followed by viraemia due to infected leukocytes (B cells, monocytes and macrophages) which disseminate the virus to bone marrow, thymus, salivary glands and reproductive organs. In the majority of cats FeLV causes a self limiting infection. But in some 30% of infected cats a persistent infection remains depending on age. They remain non-viraemic with neutralising and Feline Oncovirus Membrane Associated (FOCM) antibodies. They do not shed virus and do not develop leukaemia. However, in some cats, a persistent viremia is accompanied with high FOCMA specific antibodies. These cats develop neutralising antibodies and become healthy or the FOCMA antibodies decline and the cats develop leukaemia. Persistently infected cats are the source of disease spread. The virus is immune suppressive in those cats upon infection of T and B lymphocytes and myeloid cells. This is manifest as lymphoid or myeloid leukaemia with increased blood count of lymphoblasts or myeloblasts, respectively, and lymphosarcoma. On the other hand infection may also lead to severe immunodeficiency without lymphosarcoma development. Although the viral genome has been demonstrated in the tumours, the virus itself can be rarely isolated from such tumours. Generalised B cell tumours of lymph nodes (known as multicentric lymphosarcoma), thymic and alimentary lymphosarcomas have been observed in FeLV infected cats. In the thymic form there is marked T cell hyperplasia enlarging thymus which eventually fills most of the thoracic cavity causing dyspnoea. In the alimentary form B cell tumours develop in the wall of the intestine. These FeLV induced neoplasms may also result in haemolytic or hypoplastic anaemia, immunosuppression and reproductive failure. Infection of placenta followed by transplacental infection of foetus may result in foetal death. FIV is found worldwide in domestic cats and wild felids namely snow leopards, lions, tigers, jaguars and bobcats. FIV infection in cats has three stages, just like HIV infection in humans. The initial acute stage is characterised by fever, swollen lymph nodes, oral,
respiratory, eye and intestinal symptoms which may be recurrent or chronic in occurrence. Affected cats may have nasal and eye discharge, cloudy cornea and diarrhoea. In the second latent stage, often lasting many years the immune system is slowly destroyed leading to immunodeficiency followed by the third AIDS-like stage. Feline immunodeficiency virus is shed mainly in the saliva and the principal mode of transmission is through bites. In this perspective free-roaming animals are at the greatest risk of infection and hence FIV is uncommon in closed catteries. Sexual contact does not appear to be a significant mode of transmission although the virus may be shed in semen. The virus is transmitted to kittens from acutely infected queens through colostrum and milk [9].

4. Emergent and potential virus diseases

An important event in companion animal viral disease ecology has been the jump by contemporary strains of equine influenza H3N8 virus (Orthomyxovirus) to racing dogs first recognised during an outbreak of respiratory disease in racing greyhounds at a kennel in Florida in January 2004 [84]. In this outbreak 8 greyhounds died of haemorrhagic pneumonia while 14 remaining dogs had a milder illness manifest initially as fever and then coughing for 10–14 days. A variety of tests including genetic sequence analysis and phylogenetic comparisons led to the conclusion that all three canine flu virus isolates from January 2004 outbreak had evolved from equine influenza H3N8 virus and formed a single phylogenetic cluster. The prototype strain was then named A/canine/Florida/43/2004 (canine/FL/04). These authors also concluded that the entire (all eight RNA segments) of the horse virus had been transmitted to the dog. This may have been neither the first nor the last episode of the disease. Tests on archival dog sera and lung tissue and dog sera collected in early 2005 from various states of USA indicate occurrence of canine H3N8 influenza virus prior to and after the 2004 outbreak [84]. These authors also provide evidence of the virus’s transmissibility to pet dogs and the data suggest virus transmission by virus aerosol. Occurrence of an isolated case of canine H3N8 flu virus in the UK was identified by serology [85]. One important factor in interspecies transmission of any virus including influenza viruses is the presence of appropriate viral receptors in the respiratory tract epithelial cells of the novel host. The equine influenza haemagglutinin recognises α2,3 sialic acid linkages. Of concern would be if the new H3N8 dog flu virus became more widespread in dog populations and if it jumped to cats. The dog is also susceptible to highly pathogenic avian influenza (HPAI) virus of H5N1 subtype [86,87] and the virus was the cause of fatal dog infection in Thailand [88,86]. Susceptibility of dogs to HPAI H5N1 disease has been reproduced experimentally [87].

HPAI H5N1 virus has also jumped to domestic cats and wild felids and natural HPAI H5N1 virus infection was the cause of fatal disease in domestic cats and other large felids such as tigers and leopards in Thailand [89,90,86]. The susceptibility of domestic cats to HPAI H5N1 virus was also proven experimentally [91–93,87]. The availability of appropriate receptor(s) in the lower respiratory tract (LTR) of the novel host is an important prerequisite for the novel virus to initiate infection in the new host and cause viral pneumonia. Like the dog, cat LTR (and also human’s) has terminal 2,3-Gal linkages in the LTR [94] which are the preferred ligands for H5N1 virus and apparently also for H3N8 influenza virus.

In view of the fact that two newly emergent paramyxoviruses in the new genus henipavirus namely Hendravirus and Nipahvirus have jumped species from reservoir petropid fruit bats to man, horses and pigs in Australia and the Far East causing fatalities in all three unnatural hosts [95,96] it is important to be aware of experimental studies showing susceptibility of domestic cats to these new important pathogens. Transmission of both henipaviruses to cats is possible since infected horses and pigs shed virus oronasally [97,98]. Experimentally cats were susceptible to Hendravirus by subcutaneous, intranasal, oral inoculation and also to in contact transmission resulting in severe interstitial pneumonia, generalised thrombosis and necrosis of small blood vessels and necrotic lesions in lungs, intestine, liver and kidneys; infected cats shed virus in secretions of oropharynx and urine [99]. Oronasal inoculation of cats with a human isolate of Nipahvirus resulted in febrile respiratory and neurological disease in cats which also incurred vasculitis and haemorrhages in lymph nodes, trachea, lung and pulmonary infarcts.

Another potential cat pathogen is West Nile virus (WNV). WNV is mosquito-transmitted flavivirus belonging to the Japanese encephalitis (JE) serocomplex of the family Flaviviridae [100]. All members of the JE complex are transmitted by mosquitoes. Bird-feeding mosquitoes are the principal vectors of WNV. WNV has been isolated from 43 mosquito species mainly of the genus Culex [101]. High long-term viraemia, sufficient to infect vector mosquitoes is required for field transmission of WNV. The latter occurs in infected birds which are the principal reservoir hosts of WNV whereas mammals are less important. Bird-mosquito cycle in wetlands is the common mode of WNV transmission but bird–tick cycle in certain dry and warm habitats also occurs [101]. Importantly for this paper WNV naturally infects dogs [102–105], cats [104]. Susceptibility of dogs and cats to WNV has also been investigated experimentally [106]. Strains of WNV vary significantly in virulence for mammalian and avian species [107–109]. The insect bite results in viraemia and visceral viral replication which produces secondary viraemia which could lead to CNS infection. The visceral viral replication may cause fever, depression anorexia and some mortality while CNS replication may result in encephalitis and neurological signs such as tremors, ataxia and death [110,108,111]. Infected dogs and cats may undergo this pattern of disease pathogenesis although it is very rare for cats and dogs to be infected in the wild.

5. Immunoprophylaxis

As described earlier, vaccines are available for many years against the common well known diseases. For dog viral (and bacterial) diseases, vaccines offered by the major companies are against CDV, CAV-1 and 2, CPV, CPI-2 and rabies and some companies also for CCoV and one for CHV-1 in various combinations. For the cat vaccines are available against diseases caused by FPLV, FCV, FHV-1, FeLV, FCoV, FIPV, FIV and rabies virus. Vaccines from the companies are broadly similar in formulation and presentations (Tables 1 and 2) but vary with respect to the number of components. Furthermore, it is important to point out that some vaccine components consist of live antigens whereas others of killed. The choice between live and killed depends largely on the immunological response which is to be induced and the immunological background of the target animal (presence of maternal derived antibodies, age at which the animal is supposed to be immune, etc.) Tables 1 and 2 represent the licensures in the UK, but it should be noted here that in other countries, not all or other formulations may be licensed due to national or economic reasons. Viral vaccines are sometimes dissolved in solvents containing bacterial components such as the Leptospira spp. and Bordetella bronchiseptica antigens. In the UK, for the dog viruses the number of products ranges from 3 (Pfizer) to as many as 8 (Schering-Plough, S-P). Most companies have 5–6 products, mostly as polyvalent (multi-disease) vaccines. For the cat, the products range is 2 (S-P, Virbac), 4 (Intervet), to 6 (F-D, Merial). The reason for the multiple product range is likely to be the vaccine duration of immunity (DOI) varying from 1 year or
| Company and trade name | Vaccine | Presentation | Handling and claims |
|------------------------|---------|--------------|---------------------|
| **FORT DODGE**<br>Duramune Range | 1. PPI + L | V. LFD CPV (SAH) + CPI-5 V. K-L. | Reconstitute V. LFD with K-L and apply S/C from 6 to 10 weeks and again 3–4 weeks later. OI: from 2 weeks DOI: 1 year; CPI-5 unknown. Contra-indicated for pregnant bitches. |
| 2. PPI + LC | V. LFD: CPV (SAH) + CPI-5 (FDL) and V. K-L + K-CCoV (TN449). | As with PPI + L. OI: From 2 weeks. DOI: 1 year; CPI-5 unknown. Contra-indicated for pregnant bitches. |
| 3. DAFFPI + L | V. LFD: CDV (Onderstepoort) + CAV-2 (V197) + CPV (SAH) + CPI-5 (FDL) and V. K-L. | As with PPI + L. OI: From 2 weeks. DOI: 3 years for CDV, CAV and CPV but CPI-5 unknown. Contra-indicated for pregnant bitches. |
| 4. DAFFPI + LC | Same live viruses as 3 and V. K-L + K-CCoV (TN449). | As with PPI + L. OI: From 2 weeks. DOI: 1 year for all antigens except CPI-5. Contra-indicated for pregnant and lactating bitches. |
| 5. PPI + LC | V. LFD: CDV (Onderstepoort) + CPV (SAH) and V. K-L (TN449) and solvent. | Reconstitute V. LFD with solvent and apply S/C from 6 to 10 weeks and again 2–4 weeks later. OI: from 2 weeks. DOI: 1 year. Contra-indicated for pregnant and lactating bitches. |
| 6. Puppy DP + C | | |
| **INTERVET**<br>Nobivac Range | 1. DHP | V. LFD: CDV (Onderstepoort) + CAV-2 (Manhattan LPV3) + CPV (154) and solvent. | Reconstitute V. LFD with solvent or Nobivac Lepto2 or Nobivac Rabies and apply S/C from 6 weeks and again at 10 weeks. OI: 1 week (CDV and CPV) 2 weeks (CAV); DOI: 3 years. |
| 2. DHPPPI | Same as DHP + live CPI-5 and solvent. | As with DHP vaccine. OI: 1 week (CDV, CPV and CAV) and 4 weeks (CPI-5). DOI: 3 years (CDV, CPV and CAV); CPI-5 unknown. |
| 3. Parvo-C | V. LFD CPV and solvent. | Reconstitute as per DHP vaccine and apply S/C from 4 weeks and booster at 10 weeks but a single dose for puppies 10 weeks and older. OI: 1 week. DOI: 3 years. |
| 4. PI | V. LFD CPI-5 (Cornell) and solvent. | Reconstitute as per DHP Vaccine and apply S/C from 8 weeks and booster 2–4 weeks later. OI: 4 weeks. DOI: unknown. |
| 5. Rabies | V. K-Rabies (pasteur RIV) + Al (OH) adjuvant. | Apply S/C to dogs and cats from 4 weeks when puppies should be boosted at 3 months. OI: 2–3 weeks. DOI: 3 years. |
| **MERRIAL**<br>Eurican Range | 1. Herpes 205 | V. K-CHV-1 (F205) gB glycoprotein (0.3–1.75 μg) in oil adjuvant. | Apply S/C near or soon after mating and again 1–2 weeks before whelping and similarly at or during each pregnancy. |
| 2. DHP | V. LFD: CDV + CAV + CPV + CPI-2. | Reconstitute with Eurican L vaccine and apply S/C from 8 weeks and boost 3–5 weeks later and then annually. |
| 3. L | V. K-L | As with DHPPi. OI: 2 weeks. DOI: 1 year. |
| 4. P | V. LFD: CPV. | As with DHPPi but single injection for dogs 12 weeks and older. OI: 1 week. DOI: 1 year. |
| 5. Rabisin | V. K-Rabies with Al (OH) adjuvant. | Apply S/C to dogs and cats from 3 months and boost every 2 years. |
| **PFIZER**<br>Vangard Range | 1. 7 | V. LFD: CDV (Synder Hill) + CAV-2 (Manhattan) + CPI-5 (NL) V. LS: CPV (NL 35-D) + K-L. | Reconstitute V. LFD with V. LS + K-L and apply S/C twice 2 weeks apart to puppies 10 weeks and younger but single dose for older dogs OI: 2 weeks. DOI: 1 year (also for CAV-1) but unknown for CPI-5. Contra-indicated for pregnant bitches. |
| CPV | V. LS CPV (NL35-D). | As per Vangard 7. OI: 2 weeks. DOI: 1 year. Contra-indicated for pregnant bitches. |
| CPV-L | V. LS CPV (NL35-D) + K-L. | As per Vangard 7. Same claims as CPV vaccine. Contra-indicated for pregnant bitches. |
| **SCHERING–PLOUGH**<br>Procyon & Quantum Range | 1. Dog DA2PPI/CVL | V. LFD: CDV (Distemperoid) + CAV-2 (Ditchfield) + CPV (SAH 2b) + CPI (Philips Roxane) V. K-CCoV (FEC-SAH) + K-L. | Reconstitute V. LFD with V. K-CC + K-L and apply S/C or I/M from 6 weeks and boost 3–4 weeks later. OI: 3–4 weeks. DOI: 3 years for CDV, CAV (1 and 2) and CPV; 1 year for CPI, CCoV and Lepto serovars. |
| 2. Dog DA2PPI/L | Same as DA2PPI/CVL but without CCoV. | Same as DA2PPI/CVL vaccine for the components present including claims. |
| 3. Dog PI/CVL | V. LFD: CPI (Philips Roxane) V. K-CCoV (FEC SAH) + K-L (115 and 117). | Reconstitute as vaccines 1 and 2. Same claims for the active components present in DA2PPI/CVL. |
| 4. Dog PI/L | Same as vaccine 3 but without CCoV antigen. | Reconstitute and apply as vaccine 1. Same claims for the components present in vaccine 1. |
| 5. Dog 7 | V. LFD: CDV + CAV-2 + CPI-2 V. LS CPV + K-L. | Reconstitute V. LFD with V. LS CPV + K-L + and apply S/C twice from 10 weeks and again at 12 weeks but a single dose to older puppies and then annually. |
| 6. Dog CPV | V. LS CPV. | Apply S/C from 6 weeks and again at 12 weeks and then annually. There are other options. |
| 7. Dog CPV-L | V. LS CPV + K-L. | Apply as per Quantum CPV. |
| 8. Rabies | V. K-Rabies (Flury) suspension with Al (OH) adjuvant. | Apply S/C to dogs and cats from 3 months and then every 3 years. |
| **VIRBAC**<br>Canigen Range | 1. DHP | V. LFD CDV (Onderstepoort) + CAV-2 (Manhattan) + CPV (154) and solvent. | Reconstitute V. LFD with solvent or Canigen Lepto 2 or Canigen Rabies and apply S/C from 6 weeks and again at 12 weeks. OI: 1 week for CDV and CPV and 2 weeks. DOI: 3 years when booster recommended. |
Table 1 (Continued)

| Company and trade name | Vaccine | Presentation | Handling and claims |
|------------------------|---------|--------------|---------------------|
| 2. DHPPI               | V. LFD: CDV + CAV-2 + CPV + CPI and solvent. | Reconstitute V. LFD with Canigen Lepto 2 or solvent and apply S/C from 6 weeks and again 4 weeks later. Additional dose of Canigen PI recommended at 8 weeks. DOI: 3 years for CDV, CPV and CAV and 1 year for CPI when booster recommended. Not recommended for ferret and mink. | V. LFD: CPI and solvent. |
| 3. PI                  | V. LFD: CPI and solvent. | Reconstitute V. LFD with solvent or Canigen Lepto 2 or Canigen Rabies and apply S/C from 8 weeks and again 2–4 weeks later but a single dose 12 weeks onwards and then annual booster. OI: 4 weeks. DOI: 1 year. |
| 4. Rabies             | V. K-Rabies (Pasteur RV)+ aluminium phosphate adjuvant. | Apply S/C or I/M to dogs and cats from 3 months and then every 3 years. OI: 2–3 weeks. DOI: 3 years. |

Vaccines are sold in the UK. It is therefore possible, dependent on licensing authorisation sought by the companies, that there is variation in products and product composition available in other countries. Tables are merely a guide to actual formulations that are possible.

Abbreviations: V. = vial of; LFD = live freeze dried pellet of viruses; LS = live suspension of; I = inactivated, as liquid suspension or emulsion of; S = suspension; L = mixture of Leptospira serovars canicola and icterohaemorrhagiae; = combined with; OI = onset of immunity in weeks after the primary course of vaccination; DOI = duration of immunity in years; MDA = maternally derived antibody to antigen(s); S/C = subcutaneous; I/M = intramuscular. See text for abbreviated virus names.

less (CPV-2, FeLV) to 3 years (CDV, CAV-2, CPV and rabies virus); for most diseases one vaccine formulation would protect against diseases ranges from 5 to 8 and 2 to 5 for the dog and cat viral and bacterial diseases, respectively. It should be noted that not all companies claim DOI of 3 years for CPV disease. Also noteworthy is the fact that most, with an odd exception, of these vaccines were derived by conventional attenuation and/or inactivation processes in tissue culture some 10–20 years ago. The tissue culture technologies have been much refined to aid the production, quality (purity and control) and improved yield of active components. Another important point to mention is that these various vaccines contain different viral strains and their efficacy was assessed using different challenges (virus strains, inocula, animals) and sample analysis was using different tests. This clearly does not allow an objective analysis of their relative efficacy. Because of the age of these vaccines and the recent emergence of virulent variants of some viruses notably CPV (the 2a, 2b and 2c variants) and FCV (VS-FCV) [22,23,112] and the new respiratory coronavirus (see above for references) the need for assessment of efficacy of these now old vaccines against the newly emergent viruses is clearly necessary but would be costly. There are only limited investigations on this subject. An exception, to our knowledge, is the recent controlled study in susceptible dogs for CPV 2 component in Nobivac DHPPI (Table 1) against CPV 2c oral challenge which showed that the vaccine was fully cross protective [113]. Published information on the prevalence and the incidence of disease due to the recently recognised group 2 respiratory coronavirus [65] is limited but this could be another pathogen for which immunoprophylaxis may be needed. Domestic and scavenging dogs are a significant source of human rabies worldwide and vaccination of dogs has been highly beneficial in this respect [114]. CDV is a cause of fatal disease in many species of carnivores. CDV related viruses have been identified in seals (phocid distemper virus), dolphins, whales and porpoises [115,116], and vaccination strategies have shown some success [117]. CDV transmitted by domestic dogs was associated with fatal neurological disease in lions in Serengeti National Park in Tanzania and dog vaccination against CDV in affected areas was beneficial [118]. Although currently available live CDV vaccines are suitable for immunising domestic dogs and farmed mink. A CDV vaccine based on the Onsterstepoort strain is safe and efficacious in Lions by eliciting a protective neutralising antibody response [119]. The same vaccine has been used effectively in otters and seals (showing vaccine efficacy in the face of Phocine distemper outbreak [Intervet/Schering-Plough, unpublished]). The live vaccine safety concern and the global CDV distribution involving a wide variety of susceptible species, require new safe vaccines for the protection of wild species as well as eradication or reduction of CDV from wildlife [115]. A further requirement is strategies for wildlife vaccination as has been used for rabies and anticipated for RHDV and MV diseases of wild rabbits (see below).

Although canine H3N8 flu virus disease is quite new, plans for vaccine against it were afoot soon after the outbreak of the fatal respiratory disease [84]. These authors were working towards a vaccine for this new dog disease (personal communication by Dr. Cyanda Crawford to Allison Clark [120]. That there is commercial interest in canine H3N8 flu virus vaccine is indicated by a recent controlled efficacy study in dogs with two experimental canarypoxvirus–H3 subtypes (from two strains) live recombinant vaccine [121]. This study was a joint effort by Merial, Sanofi Pasteur and Cornell University.

For the cat there are FCV vaccines from several companies (Table 2) but their efficacy against the newly emergent VS-FCV [35,112] remains unknown. The development of vaccines against FIP coronavirus (FIPV) has proved cumbersome and consequently there is only one (Pfizer’s, not in Table 2) live intranasal temperature sensitive (TS) vaccine licensed in some countries [122,123]. However efficacy of this TS FIPV vaccine is a matter of debate [124,125]. A promising experimental onoral live FIPV vaccine lacking group-specific gene cluster 3abc, derived by site directed mutagenesis of a virulent lethal FIPV strain was an innocuous efficacious vaccine [126]. Clearly there is a way to derive an effective FIPV vaccine. The observation that cats can recover naturally from FeLV infection led to development of vaccines (see Table 2). These however are not fully protective [127–129]. Thus there is an ongoing effort to develop improved effective FeLV vaccines. The target is for a vaccine that would prevent establishment of both viraeemia and latent bone marrow infection. The approaches investigated have been vaccinia-FeLV [130], canarypox-FeLV [131] and FHV-1-FeLV [132] live vector
### Table 2
Feline viral disease vaccines.

| Company and trade name | Vaccine | Presentation | Handling and claims |
|------------------------|---------|--------------|---------------------|
| FORT DODGE             |         |              |                     |
| Fevaxyn & Katavac      | FELV    | V. K-FELV (A78) + adjuvant. | Apply twice S/C 3–4 weeks apart from 9 weeks and boost annually. Can be used to reconstitute Katavac CHP. |
|                        | ICHP    | V. K-FPLV + FHV-1 + FCV + mineral oil adjuvant. | Apply twice S/C 3–4 weeks apart from 8 weeks and then annually. |
|                        | 4.     | V. K-FPV + FHV-1 + FCV + Chlamyphila psittaci + mineral oil adjuvant. | As ICHP from 8 weeks. |
|                        | 5.     | V. LFD: FCV + FHV-1 + PPLV and solvent. | As ICHP from 9 weeks. |
|                        |         |              |                     |
| 6. KATAVAC ECLIPSE     | FELV    | V. LFD: FCV + FHV-1 + PPLV and solvent. | Reconstitute V. LFD in solvent or Fevaxyn FELV and apply S/C to kittens from 9 weeks but once to cats 12 weeks and older. Reconstitute V. LFD with V.K-Felv and apply twice S/C 3–4 weeks apart from 9 weeks and boost annually. |
| INTERVET               | Nobi-   |              |                     |
| vac                    | DUCAT*  | V.LFD: FHV-1 (G2620A) + FCV (F9) and solvent. | Reconstitute with solvent or Nobivac Rabies (Table 1) and apply S/C to cats from 8 weeks onwards and again 3–4 weeks later and boost annually. |
|                        | FELV    | V. Subunit p45 Felv envelope + Al (OH) and Quil A. | Apply S/C or I/M twice from 9 weeks onwards 3 weeks apart and boost annually. Oil: 3–4 weeks. Reconstitute V. LFD with Nobivac Felv or Rabies and solvent or apply S/C twice 3–4 weeks apart 9 weeks onwards and boost annually. Oil: 3–4 weeks. DOI: 1 year (FHV-1, FCV and C. Felis) and 3 years (PPLV). |
|                        | FORCAT  | V. LFD: FHV-1 (G2620A) + FCV (F9) + PPLV (MW-1) + Chlamyphila felis (Baker). | As with FORCAT. OI: 1 week (all antigens). |
| Merial Purevax         | FELV    | V. Suspension of live Canarypox (vCP97)-Felv recombinant and solvent. | Apply S/C twice 3–5 weeks apart from 8 weeks and boost annually. Contra-indicated for pregnant animals but indicated for lactating cats. |
|                        | 2.     | V. LFD: FHV-1 (F2) + K-FCV (431 and G1) and solvent. | As with FELV. For high levels of MDA delay vaccination to 12 weeks and primary course booster 3–4 weeks later. |
|                        | 3.     | V. LFD: FHV-1 (F2) + PPLV (PLIV) + K-FCV (431 and G1) and solvent. | As with RC. |
|                        | 4.     | V. LFD: FHV-1 (F2) + PPLV (PLIV) + C. felis (905) and solvent. | As with RCP from 8 weeks. |
|                        | 5.     | V. LFD: FHV-1 (F2) + PPLV + C. felis (905) + Canarypox-Felv + K-FCV (431 and G1) and solvent. | As with RC or RCP. |
|                        | 6.     | V. LFD FHV-1 (F2) + PPLV (PLIV) + Canarypox (vCP97)-Felv recombinant + K-FCV (431 and G1) and solvent. | As with RC or RCP. |
| Pfizer Felocell        | CVR     | V. LFD: PPLV (snow leopard strain) + FHV-1 (FVRm) + FCV (F9) and solvent. | Reconstitute V. LFD with solvent and apply S/C twice 3–4 weeks apart from 9 weeks and boost annually. Contra-indicated for pregnant queens. |
| SCHERING-PLough        | CVRP    | V. LFD FCV + FHV-1 + PPLV and solvent. | Reconstitute V. LFD with solvent or Quantum cat Felv and apply S/C twice 3–4 weeks apart from 9 weeks and boost annually. Contra-indicated for pregnant cats. Oil: 3 weeks. DOI: 1 year. |
| Quantum Range          |         |              |                     |
|                        | Cat FELV | Suspension of subunit FeLV glycoprotein 70 and FOCMA antigens + adjuvant. | As with Quantum CVRP but safe for pregnant cats. Oil: 3 weeks. DOI: 1 year. |
| VIRBAC                 | RCP     | V. LFD: FPLV (DSV LR 72) + FHV-1 (F2) + FCV (F9) and solvent. | Reconstitute V. LFD with solvent or Leucogen and apply twice S/C from 9 weeks and again 2 weeks later and then annually. Contra-indicated in pregnancy. |
|                        | Leucogen| V. p45 Felv envelope antigen expressed in E. coli + Al (OH) and Quil A as adjuvants. | Apply S/C or I/M twice from 9 weeks and again 2–3 weeks later and then annually. Recommended for queens prior to mating. |

See Table 1 text for rabies virus vaccine for immunising cats. See legend of Table 1.

Vaccines. The vaccinia-Felv vaccine was ineffective while the other two live vector vaccines were not better than existing vaccines. However, experimental vaccines that showed excellent protection were the Felv iscoms [133] and FeLV DNA co-administered with interleukin 12 (IL-12) and IL-18 cytokine genes [134].

FIV is a cause of significant disease in domestic cats worldwide. Immunoprophylaxis for FIV disease is limited and only one company (F-D) offers a vaccine, approved in spring 2002. Currently the use of the vaccine is not recommended by The American Association of Feline Practitioners. Like its human counterpart, the
immunodeficiency virus of human AIDS, FIV presents a formidable challenge for vaccine development despite a vigorous host immune response to the virus. Various approaches for a vaccine have been investigated [135] with some success. It has been shown that a multi-epitopic vaccine for instance does induce an immune response which is not protective [136]. An important difficulty has been the strain specificity of vaccines in that experimental vaccines were not protective for heterologous strains [137]. The newly emerged HPAI H5N1 induced viral disease in dogs and cats is clearly a new challenge for the institutional and industrial virologists to develop yet another vaccine. In this regard a conventional killed adjuvanted H5N6 flu virus vaccine was protective against lethal HPAI H5N1 experimental challenge in a controlled efficacy study in cats [93].

Booster vaccination after the primary course and DOI is an important issue in the recent vaccination debate particularly for the dog and cat vaccines. However, the time for the booster vaccination is difficult to assess since (i) response of individual animals to routine vaccination is highly variable which is also influenced by the level of MDA at primary vaccination, (ii) the frequency of field exposure is often unknown and (iii) products vary with respect to potency and formulation. Antibody test may be appropriate for establishing residual immunity for some antigens but not all and the cost is likely to exceed that of booster vaccination [138]. However, in general, for the so-called core dog vaccines for CAV-2, CDV, CPV and rabies and cat vaccines for FPLV, FCV, FHV-1 and rabies published data suggest a minimum DOI of 3 years [139]. Therefore for these core vaccines a general vaccination guideline should be first vaccination at as early as 6 weeks of age or older (>12 weeks) depending on disease and available vaccine type (live versus killed), then again at 1 year and then every 3 years. For the non-core vaccines yearly boosters are recommended. Animals with high MDA may require two vaccinations in the primary vaccination regimes.

For rabbits, diseases covered by vaccine companies are those due to RHDV and MV but the choice of vaccines is rather limited (Table 3). For RHDV CEVA and F-D have a similar formulation of rabbit grown liver antigen [140,141] plus oil adjuvant. Since RHDV has failed to grow in tissue culture, various expression vectors have been developed for the production of RHDV capsid VP60 protein. These vectors comprise E. Coli [142], Saccharomyces cerevisiae [143], poxviruses: myxoma [144], vaccinia [145], canarypox [146]. VP60 was also produced in rabbit kidney cell line RK-13 [147] and potato [148] and baculovirus [149]. Many of the vector expressed VP60 antigens incorporated into experimental vaccines were immunogenic and protective for rabbits against fatal RHDV challenge [150]. Commercially only one MV disease for domestic rabbits is marketed by Intervet (Table 3). The latter is a live heterotypic vaccine based on less pathogenic leporipox Shope fibroma virus. For both RHDV and MV diseases a key requirement is vaccines which could be used for both domestic and wild rabbits. The latter play an important ecological role in Mediterranean and other ecosystems. This entails a strategy for wildlife immunisation which is feasible as has been achieved for sylvatic rabies control in Europe and North America by oral vaccines delivered by baiting [151–153]. Other methods are delivery by biting insects and/or by direct horizontal animal to animal vaccine spread. All these three modes of vaccination against RHDV and MV diseases were elegantly demonstrated by controlled experimental challenge studies [150]. However we do wonder if such a vaccine would indeed be commercialised.

6. Conclusions

The main conclusions we draw from the above account of important viral diseases of cats, dogs and rabbits are:

1. Viruses from several different families naturally infect these companion animals and cause significant disease. Most of the viruses are transmitted via the oropharyngeal route by virus shed in secretions of saliva, nasal mucus, aerosol and/or faeces. Virus in secretions is inhaled and/or ingested and initiates primary replication in mucosa of the respiratory and/or intestinal tracts; rabbits virus shed in saliva, is however delivered to myocytes, the site of primary replication, via bite while myxomavirus is trans-

---

### Table 3

| Company and trade name | Vaccine | Presentation | Handling and claims |
|------------------------|---------|--------------|---------------------|
| **Rabbit and Pigeon viral disease vaccines.** | | | |
| **Vaccines for rabbits** | | | |
| CEVA | Lapinject VHD | V. K-RDDV (P174) + oil adjuvant. | Apply S/C from 5 weeks and boost annually. OI: 6 days. DOI: 1 year. Safe for pregnant rabbits. |
| FORT DODGE | Cylap | V. K-RHDV + oil adjuvant. | Apply twice S/C from 2.5 to 3 months and 4 weeks later and then annually. Safe for pregnant rabbits. |
| INTERVET Nobivac | Myxo | V. LFD: Shope fibroma virus and solvent. | Reconstitute V. LFD with solvent and virus and solvent and apply intra dermally or S/C from 6 weeks and older rabbits. OI: 2 weeks and DOI: 6 months. Contra-indicated for breeding and pregnant rabbits. |
| **Vaccines for pigeons** | | | |
| FORT DODGE Colombovac Range | 1. PMV | V. K-PMV-1 + adjuvant. | Apply S/C to racing and show pigeons from 3 weeks and then annually. Adult birds can be similarly vaccinated. |
| | 2. PMV/POX | V. LFD PPV V. K-PMV-1 + adjuvant. | Reconstitute V.LFD PPV with V. K-PMV-1 and apply S/C to racing and show pigeons from 6 weeks and then annually. Adult birds can be similarly vaccinated. |
| INTERVET | NOBILIS PARAMYXO | V. K-PMV-1 + mineral oil adjuvant. | Apply S/C from 6 weeks before race or exhibition and then annually. OI: 4 weeks. DOI: 1 year. |

See legend of Table 1.
mitted by blood feeding arthropod vectors such as mosquitoes, fleas and others in addition to inhalation of virus.

2. In disease pathogenesis an important determinant for significant disease is if the virus is able to infect leukocytes and then be disseminated to internal organs for secondary replication and cause pathology. However most cat and dog coronaviruses are generally restricted to the primary site of infection and cause acute, self-limiting mild enteric or respiratory disease. Virotropic virulent strains also occur naturally with variable frequency following mutational changes. Examples are FCoVs causing infectious peritonitis and the recent cases of genotype 2 CCpV strain CB/05 disease in dogs. Like the coronaviruses, most calicivirus infections of cats are limited to the respiratory tract resulting in self-limiting disease but recent emergence of viretropic VS-FCV variants cause severe disease in cats and the disease pathogenesis has similarities to the usually fatal disease of rabbits due to RHDV. Leukocyte-associated viraemia is also important in parvovirus disease of cats and dogs and related wild felids and canids.

3. The tropism for enteric epithelium and virus survival in faces has been important in evolution of the carnivore parvoviruses. CPV has naturally evolved relatively rapidly and the small evolutionary changes have been in virus capsid VP2 gene and interestingly were associated with the loss and then renovation of the feline host range.

4. For the established viruses of the cats and dogs there is a good choice of vaccines developed 10–20 years ago. Hence, they are due for re-assessment for their efficacy for some components notably the newly emergent CPVs and VS-FCV. There is however the need for improved vaccines for FIPV, FeLV and FIV. This is also the case for MV and RHDV vaccines for rabbits. Also needed is RHDV vaccine for wild rabbits.

5. The recent emergence of HPAI H5N1 disease in cats and other large felids and that of H3N8 equine influenza virus in dogs are significant developments and may require vaccines should the viruses get established in these novel hosts and spread more widely. Also we should be aware that cats and dogs have the potential to acquire new viral diseases for example those due henipa parvomyxoviruses.

Acknowledgements

We are grateful to Miss Hanny van Lare for typing the reference list. J.P.’s thanks to Miss Susan Didlick for help with tricky computer manoeuvres. We gratefully thank Professor Dr. Peter Rottier and Dr. Herman Egberink (University of Utrecht, Faculty of Veterinary Medicine, NL) and Drs. Jac Bergman and Stuart Chalmers (Intervet Schering Plough Animal Health) for their time and critical comments on the subject of this article.

References

[1] Patel JR, Heldens JC. Equine herpesvirus 1 (EHV-1) and 4 (EHV-4) - epidemiology, disease and immunoprophylaxis: A brief review. The Veterinary Journal 2005;170(1):14–23.
[2] Heldens JC, Patel JR, Chanter N, Ten Thij GJ, Gravendijck M, Schijns VE, et al. Veterinary vaccine development from an industrial perspective. Veterinary Journal 2008;178:7–20 [Epub ahead of print].
[3] Patel JR, Heldens JC. Immunoprophylaxis against important virus diseases of horses, farm animals and birds. Vaccine, submitted for publication.
[4] Marlier D, Vindevogel H. Viral infections in pigeons. Veterinary Journal 2006;172(1):40–51.
[5] Rozman B, Desoubray RC, Fleckenstein B, Lopez C, Minson AC, Studdert MJ. Family herpesviridae. In: Murphy FA, Faustett CM, Bishop DHL, Ghabrial SA, Jarvis AW, Martell GP, Mayo MA, Summers MD, editors. Virus Taxonomy, 6th report of the International Committee on Taxonomy of Viruses. Archives of Virology, Wien, New York: Springer-Verlag; 1995, p. 314–27 [Supplement 10].
[6] Meyer G, Lemaire, Lyaka J, Fastetop PT, Thiry E. Establishment of a rabbit model for bovine herpesvirus type 5 neurological acute infection. Veterinary Microbiology 1996;51:27–40.

[7] Patel JR, Didlick SD. Epidemiology, disease and control of infections in ruminants by herpesviruses—an overview. Journal of South African Veterinary Association 2008;79(1):8–14.
[8] Schack A, Reid HW. Characterisation of the lymphoproliferation in rabbits experimentally affected with malignant catarrhal fever. Veterinary Microbiology 1996;53:1–2; 111–9.
[9] Murphy FA, Gibbs EPJ, Horzinek MC, Studdert MJ. Veterinary virology. 3rd ed. London: Academic Press; 1999.
[10] Virusatxonomy: classification and nomenclature of viruses. Murphy FA, Faustett CM, Bishop DHL, Ghabrial SA, Jarvis AW, Martell GP, Mayo MA, Summers MD, editors. Sixth report of the international committee for the taxonomy of viruses. Archives of virology. Vienna, Austria: Springer-Verlag; 1995 [Supplement 1E].
[11] Fennor F, Ross J. Myxomatosis. In: Tompson HV, King CM, editors. The European rabbit. The history and biology of a successful coloniser. Oxford, England: Blackwell Scientific Publications; 1994, p. 205–40.
[12] Kerr PJ, Best SM. Myxoma virus in rabbits. Reviews of Scientific and Technical Office of OIE 1998;17:256–68.
[13] Matsunaga Y, Chino F. Experimental infection of young rabbits with rabbit parvovirus. Archives of Virology 1981;68:3–14:257–62.
[14] Parrish CR, Carmichael LE. Antigenic structure and variation of canine parvovirus type-2, feline panleukopenia virus, and mink enteritis virus. Virology 1983;129:2; 401–14.
[15] Ikeda Y, Nakamura K, Miyazawa T, Takahashi E, Mochizuki M. Feline host range of canine parvovirus: recent emergence of new antigenic types in cats. Emerging Infectious Diseases 2002;8(4):341–6.
[16] Hughey WR. An enteric disease of dogs resembling feline panleukopenia. Australian Veterinary Journal 1978;54:12; 593.
[17] Appel MJ, Cooper BJ, Greisen H, Scott F, Carmichael LE. Canine viral enteritis. I. Status report on corona- and parvo-like viral enteritis. Cornell Veterinarian 1979;69:123–33.
[18] Kelly WR, Atwill RB. Diffuse subacute myocarditis of possible viral aetiology: a case of sudden death in pups. Australian Veterinary Journal 1979;55:3; 36–7.
[19] Gumbrell RC. Parvovirus infection in dogs. New Zealand Veterinary Journal 1979;27(6):113.
[20] Parrish CR, Aguado CR, Strasheim LM, Evermann JF, Sgro J-Y, Mohammed HO. Rapid antigenic-type replacement and DNA sequence evolution of canine parvovirus. Journal of Virology 1991;65:6454–52.
[21] Parrish CR. The emergence and evaluation of canine parvovirus—an example of recent range mutation. Seminars in Virology 1994;5:121–32.
[22] Truyen U, Cruenberg A, Chang SF, Obermaier B, Veijalainen P, Parrish CR. Evolution of the feline-subgroup paroviruses and the control of canine host range in vivo. Journal of Virology 1999;63(8):4702–10.
[23] Truyen U, Platzer G, Parrish CR. Antigenic type distribution among canine paroviruses in dogs and cats in Germany. Veterinary record 1996;138:365–6.
[24] Parrish CR, O’Connell PH, Evermann JF, Carmichael LE. Natural variation of canine parvovirus. Science 1985;230(4729):1046–8.
[25] Steinel A, Munson L, van Vuuren M, Truyen U. Genetic characterization of feline parovirus sequences from various carnivores. Journal General Virology 2000;81:345–50.
[26] Buonavoglia C, Martella V, Pratelli A, Tempesta M, Cavalli A, Buonavoglia D, et al. Evidence for evolution of canine parvovirus type-2 in Italy. Journal of General Virology 2001;82:3021–5.
[27] Nakamura M, Tohya Y, Miyazawa T, Mochizuki M, Phung HTT, Nguyen NH, et al. A novel antigenic variant of canine parvovirus from a Vietnamese dog. Archives of Virology 2004;149:2261–9.
[28] Ikeda Y, Mochizuki M, Naito R, Nakamura K, Mikami T, Takahashi E. Predominance of canine parvovirus (CPV) in unvaccinated cat populations and emergence of new antigenic types of CPV in cats. Virology 2000;278(1):13–9.
[29] Gamoh K, Shimazaki Y, Makie H, Senda M, Itoh O, Inoue Y. The pathogenicity of canine parvovirus type 2b, FP84 strain isolated from a domestic cat, in domestic cats. Journal of Veterinary Medical Science 2003;65:1027–9.
[30] Pollock RV, Carmichael LE. Canine viral enteritis. Veterinary Clinics North American Small Animal Practice 1983;13(3):551–66.
[31] Evermann JF, McKeirnian AJ, Smith AM, Skilling DE, Ott RL. Isolation and identification of caliciviruses from dogs with enteric infections. American Journal of Veterinary Research 1985;46(1):218–20.
[32] Schaffer FL, Soergel ME, Black JW, Skilling DE, Smith AM, Cubitt WD. Characterization of a new calicivirus isolated from feces of a dog. Archives of Virology 1985;84(3–4):181–95.
[33] Mochizuki M, Kawanishi A, Sakamoto H, Tashiro S, Fujimoto O, Ohwaki M. A calicivirus isolated from a dog with fatal diarrhoea. Veterinary Record 1993;132(9):221–2.
[34] Pratelli A, Groco G, Camero M, Corrente M, Normanno G, Buonavoglia C. Isolation and identification of a calicivirus from a dog with diarrhoea. New Microbiology 2000;23(3):257–60.
[35] Pedersen NC, Elliot JB, Glasgow A, Poland A, Keel K. An isolated epizootic hemorrhagic-like fever in cats caused by a novel and highly virulent strain of feline calicivirus. Veterinary Microbiology 2000;73:281–300.
[36] Radford A, Coyne K, Dawson S, Porter C, Gaskell R. Feline calicivirus. Veterinary Research 2007;38:319–35.
[37] Osellio R, Sheh A, Shetterly L, Pesavento P, Parker J. Feline caliciviruses (FCVs) isolated from cats with virulent systemic disease possess in vitro phenotypic differences from those of other FCV isolates. Journal of General Virology 2007;88:506–17.
[38] Kate F, Pasavento PA, Pederson NC, Poland AM, Wilson E, Foley JE. An outbreak of virulent systemic feline calicivirus disease. Journal of the American Veterinary Medical Association 2004;224:241–9.

[39] Pasavento PA, MacLaughlin DJ, Dillard-Telm L, Grant CK, Hurley KE, et al. Pathologic, immunohistochemical and electron microscopic findings in naturally occurring virulent systemic feline calicivirus infection in cats. Veterinary Pathology 2004;41:257–326.

[40] Coyne K, Dawson S, Radvord A, Cripps P, Portes C, McCraken C, et al. Long-term analysis of feline calicivirus prevalence and virulent shedding patterns in naturally infected colonies of domestic cats. Veterinary Microbiology 2008;118:12–25.

[41] Liu S, Xue HP, Pu BQ, Qan SH. A new viral disease in rabbits. Animal Husbandry and Veterinary Medicine 1984;16:253–5.

[42] Gustafson K, Svensson T, Ugglu A. Studies on idiopathic syndrome in the brown hare (Lepus europaeus P.) and mountain hare (Lepus timidus L.) in Sweden, with special reference to hepatic lesions. Journal of Veterinary Medicine A 1989;36:631–7.

[43] Moussa A, Chasse D, Lavazza A, Cappucci I, Smid B, Meyers G, et al. Haemorrhagic disease of lagomorphs: evidence for a calicivirus. Veterinary Microbiology 1992;33:375–81.

[44] Fenner F, Fantini B. Biological control of vertebrate pets. The history of myxomatosis—an experiment in evolution. Walthamford, Oxford: CAB International; 1999. pp. 237–272 [chapter 11].

[45] Cooke BD. Rabbit haemorrhagic disease: field epidemiology and the management of wild rabbit populations. Scientific and Technical Review (International Office of epizootics) 2002;21:347–58.

[46] Groneberg DA, Hilgenfeld R, Zabel P. Molecular mechanisms of severe acute respiratory syndrome. Current Topics in Microbiology and Immunology 2002;283:123–30.

[47] Fuchs A, Weissenböck H. Comparative histopathological study of rabbit haemorrhagic disease. Journal of Veterinary Medicine A 1992;39:273–9.

[48] Pasavento PA, MacLachlan NJ, Dillard-Telm L, Grant CK, Hurley KE, et al. Pathologic, immunohistochemical and electron microscopic findings in naturally occurring virulent systemic feline calicivirus infection in cats. Veterinary Pathology 2004;41:257–326.

[49] Coyne K, Dawson S, Radvord A, Cripps P, Portes C, McCraken C, et al. Long-term analysis of feline calicivirus prevalence and virulent shedding patterns in naturally infected colonies of domestic cats. Veterinary Microbiology 2008;118:12–25.

[50] Liu S, Xue HP, Pu BQ, Qan SH. A new viral disease in rabbits. Animal Husbandry and Veterinary Medicine 1984;16:253–5.

[51] Kipar A, Köhler K, Leukert W, Reinacher M. Evaluation of lymphatic tissue and accessory lymphoid organs in naturally infected colonies of domestic cats. Veterinary Microbiology 1992;33:375–81.

[52] Fenner F, Fantini B. Biological control of vertebrate pets. The history of myxomatosis—an experiment in evolution. Walthamford, Oxford: CAB International; 1999. pp. 237–272 [chapter 11].

[53] Cooke BD. Rabbit haemorrhagic disease: field epidemiology and the management of wild rabbit populations. Scientific and Technical Review (International Office of epizootics) 2002;21:347–58.

[54] Pasavento PA, MacLachlan NJ, Dillard-Telm L, Grant CK, Hurley KE, et al. Pathologic, immunohistochemical and electron microscopic findings in naturally occurring virulent systemic feline calicivirus infection in cats. Veterinary Pathology 2004;41:257–326.

[55] Coyne K, Dawson S, Radvord A, Cripps P, Portes C, McCraken C, et al. Long-term analysis of feline calicivirus prevalence and virulent shedding patterns in naturally infected colonies of domestic cats. Veterinary Microbiology 2008;118:12–25.

[56] Liu S, Xue HP, Pu BQ, Qan SH. A new viral disease in rabbits. Animal Husbandry and Veterinary Medicine 1984;16:253–5.

[57] Kipar A, Köhler K, Leukert W, Reinacher M. Evaluation of lymphatic tissue and accessory lymphoid organs in naturally infected colonies of domestic cats. Veterinary Microbiology 1992;33:375–81.

[58] Fuchs A, Weissenböck H. Comparative histopathological study of rabbit haemorrhagic disease. Journal of Veterinary Medicine A 1992;39:273–9.

[59] Pasavento PA, MacLachlan NJ, Dillard-Telm L, Grant CK, Hurley KE, et al. Pathologic, immunohistochemical and electron microscopic findings in naturally occurring virulent systemic feline calicivirus infection in cats. Veterinary Pathology 2004;41:257–326.

[60] Coyne K, Dawson S, Radvord A, Cripps P, Portes C, McCraken C, et al. Long-term analysis of feline calicivirus prevalence and virulent shedding patterns in naturally infected colonies of domestic cats. Veterinary Microbiology 2008;118:12–25.

[61] Liu S, Xue HP, Pu BQ, Qan SH. A new viral disease in rabbits. Animal Husbandry and Veterinary Medicine 1984;16:253–5.

[62] Kipar A, Köhler K, Leukert W, Reinacher M. Evaluation of lymphatic tissue and accessory lymphoid organs in naturally infected colonies of domestic cats. Veterinary Microbiology 1992;33:375–81.

[63] Fuchs A, Weissenböck H. Comparative histopathological study of rabbit haemorrhagic disease. Journal of Veterinary Medicine A 1992;39:273–9.

[64] Pasavento PA, MacLachlan NJ, Dillard-Telm L, Grant CK, Hurley KE, et al. Pathologic, immunohistochemical and electron microscopic findings in naturally occurring virulent systemic feline calicivirus infection in cats. Veterinary Pathology 2004;41:257–326.

[65] Coyne K, Dawson S, Radvord A, Cripps P, Portes C, McCraken C, et al. Long-term analysis of feline calicivirus prevalence and virulent shedding patterns in naturally infected colonies of domestic cats. Veterinary Microbiology 2008;118:12–25.

[66] Liu S, Xue HP, Pu BQ, Qan SH. A new viral disease in rabbits. Animal Husbandry and Veterinary Medicine 1984;16:253–5.
[150] Barcena J, Morales M, Vazquez B, Boga JA, Parra F, Lucientes J, et al. Horizontal transmissible protection against myxomatosis and rabbit hemorrhagic disease by using a recombinant myxoma virus. Journal of Virology 2000;74:1114–23.

[151] Brochier B, Aubert MF, Pastoret PP, Masson E, Schon J, Lombard M, et al. Field use of a vaccinia-rabies recombinant vaccine for the control of sylvatic rabies in Europe and North-America. Scientific and Technical Review (OIE) 1996;15:947–70.

[152] Pastoret PP, Brochier B. The development and use of a vaccinia-rabies recombinant oral vaccine for the control of wildlife rabies: a link between Jenner and Pasteur. Epidemiology and Infection 1998;116:235–40.

[153] Niin E, Laine M, Guiot AL, Demerson JM, Cliquet F. Rabies in Estonia: situation before and after the first campaigns of oral vaccination of wildlife with SAG2 vaccine bait. Vaccine 2008;26:3556–65.