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Literature Review: Epidemiological Assessment, Prevalence & Control Measures for Canine Parvoviruses in Europe

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List of abbreviations

- CPV: Canine parvovirus.
- GALT: Gut-associated lymphoid tissue.
- MDA: Maternally derived antibodies.
- MLV: Modified live virus.
- VP: Viral protein.
- Mabs: Monoclonal antibodies.
- aa: Amino acids.
- IgG: Immunoglobulin G.
- HI: Haemagglutination inhibition.
- WSAVA: World small animal veterinary association.
- FPV: Feline panleukopaenia virus.
- UK: United Kingdom.
- WOAH: World Organisation for Animal Health.
- HIV: Human immunodeficiency virus.
- PCR: Polymerase chain reaction.
- PPE: Personal protective equipment.
- JRT: Jack Russell terrier

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Introduction

Canine parvovirus (CPV) is a virus stemming from the genus Parvovirus, family name Parvoviridae. It can be a deadly virus for unvaccinated puppies & adult dogs as well as puppies & adult dogs who have not finished their primary course of core vaccinations. It is thought the virus is a mutation of the feline panleukopaenia virus. Upon infection, the virus replicates in the lymphoid tissues of the throat and the gut-associated lymphoid tissue (GALT) leading to a viraemia in all tissues, especially rapidly dividing cells. The most important cells affected include crypt cells of the small intestine, myocardial cells, and lymphoid tissues. This leads to the manifestation of symptoms such as haemorrhagic diarrhoea, dehydration, gastroenteritis & dyspnoea. The disease has a high mortality rate in young unvaccinated puppies and the virus remains a threat despite vaccinations.

CPV-2 was first described in 1978 by Dr. L. Carmichael & Dr. M. Appel of The Baker Institute in the United States. Since then it has mutated to produce 3 mutants. The first mutant was first described in 1979 and was called CPV-2a. Subsequently, CPV-2b & CPV-2c were described in 1984 & 2000 respectively. All three variants of CPV-2 can be found in Europe, but not in all countries. There are control measures in place throughout the continent to reduce transmission of the virus among the dog population. A series of vaccinations are available under different brand names. Core vaccinations cover vaccination against CPV-2 and modified live virus (MLV) vaccinations are routinely used in practice. Once an animal is diagnosed with CPV-2, a series of measures are undertaken such as biosecurity and isolation of the patient during treatment.

The objective of this thesis is to compile existing scientific studies of CPV-2 & its variants. To take a look at their distribution within Europe. To examine CPV-2 & its characteristics & to discuss the history of CPV-2 & the emergence of its variants along with mentioning the most significant individuals who first described these viruses. Recommended vaccination protocols will be reviewed, and the failures of vaccination will be discussed. We will also examine the breed and gender distribution among patients.

Literature review

Canine Parvovirus: Overview & Characteristics

Parvoviridae is composed of two subfamilies, Densovirinae & Parvovirinae. Parvovirinae infects vertebrates while Densovirinae infects arthropods. There are five genera: Amdovirus, Bocavirus, Dependovirus, Erythrovirus & Parvovirus. CPV-2 belongs to the genus Parvovirus (Decaro & Buonavoglia, 2012). Parvoviruses are single stranded DNA viruses which have a diameter of 25 nm, are approximately 5 kilobases, (Cságola, et al., 2014) are non-enveloped, have a spherical capsid comprised of three proteins: viral protein (VP) 1, VP2 & VP3 (Decaro & Buonavoglia, 2012). CPV-2 replicates in the nuclei of rapidly dividing cells such as those in the gastrointestinal tract and myocardium, therefore intranuclear inclusion bodies are formed (Singh, et al., 2022). CPV-2 is highly stable in the environment, displaying resistance against temperature, pH changes & disinfectants for months (Decaro & Buonavoglia, 2012).

Infection occurs when a susceptible animal comes into contact with faecal material from an infected host via the faecal-oral or faecal-nasal route. CPV-2 binds to the cell via a transferrin receptor (Hafenstein, et al., 2007).

Canine Parvovirus 1 (CPV-1) was first discovered in 1967 (Humm & Hughes, 2009). This virus is more commonly known as Canine Minute Virus or Canine Bocaparvovirus 1 which is known to cause mild diarrhoea. In 1978, Canine Parvovirus 2 (CPV-2) was discovered, it was seen to cause a more acute diarrhoea which was haemorrhagic in some instances (Humm & Hughes, 2009). The disease resembled Feline Panleukopaenia with a similarity of 98%, showing a difference in amino acids in the capsid protein of the virus (Chang, et al., 1992). In 1979, a subtype, CPV-2a was recognised & five years later, CPV-2b was recognised (Humm & Hughes, 2009). Due to virus characteristics, another subtype, CPV-2c was identified in 2000 in Italy. This subtype has been detected throughout the United States, Europe, South America, and parts of Asia. In 1996, CPV-2c strain was isolated in Germany which provided evidence of the variant circulating before its primary detection in Italy (Sutton, et al., 2013). To date, CPV-2c has not been recorded in Ireland (McElligot, et al., 2011). There is conflicting evidence that the latest subtype is more pathogenic than CPV-2b & whether or not it has higher mortality rates. These antigenic variants are distinguished using monoclonal antibodies (MAbs) & have replaced CPV-2 (Decaro & Buonavoglia, 2012). CPV-2a & CPV-2b are different to CPV-2 due to differing amino acid (aa) in the VP2 protein of the capsid as seen in figure 1 provided by Decaro, et al., 2012.

CPV-2 is a highly virulent virus with an average morbidity of 100% & a mortality rate of 90% in untreated cases, if treated this rate can be as low as 13.4% according to Horecka, et al., 2020, the disease usually infects unvaccinated and partially vaccinated dogs between the ages of six weeks & six months old. In unvaccinated dogs over the age of six months it is more likely intact males will be infected, which may be an over representation. (Houston, et al., 1996) During a puppy's first few weeks of life they are protected from CPV-2 due to maternal antibodies derived from their dam's colostrum & only 10% of antibodies are derived from transplacental origin. (Mila, et al., 2014). As a puppy's maternally derived antibodies (MDA) to CPV-2, mainly in the form of immunoglobulin G (IgG) (Decaro, et al., 2020), begin to decrease, they are more susceptible to infection. According to Pollock, et al., 1982, puppies with haemagglutination-inhibition (HI) titres less than 1:80, are no longer protected against CPV-2. A study by Mila, et al., 2014 showed that MDA had a half-life of 13.4 days, and the MDA may block immunisation by vaccination in puppies with HI titres of > 1:20. This is due to neutralisation of the vaccine antigens by MDA. According to Decaro, et al., 2020 there is an immunity gap which lasts two to three weeks. During this period the MDA begin to decrease, in this time the puppy is susceptible to CPV-2 infection but can still neutralise the antigens found in vaccines. According to Decaro, et al., 2020 a series of actions have been suggested to avoid this interference, including high-titre vaccines, MDA titre determination & finding alternative vaccination routes. The idea behind high titre vaccines is that the administered vaccines will have a 2-3 logs higher viral titre compared to traditional vaccines in which case the MDA will not neutralise all antigens which can then evoke an immune response. Other routes of administration have been suggested such as intranasal & oral, but these methods are off-label and according to the World Small Animal Veterinary Association (WSAVA) are not as effective as a subcutaneous vaccination. Lastly, determining MDA titres has been suggested but this is bothersome in the sense it would require collection & testing of serum from all puppies which is not feasible in the field (Decaro, et al., 2020). Another downfall of vaccination is that some patients do not respond to the vaccines & are not shown to have enough detectable antibodies even after their primary core vaccinations. The Rottweiler and the Dobermann Pinscher have been reported to be at a higher risk of immunisation failure to CPV-2 vaccines according to Houston, et al., 1996.

Aa residue	80	87	93	101	103	232	297	300	305	323	375	426	555	564	568
Nt position	**3024-3026**	**3045-3047**	**3063-3065**	**3087-3089**	**3093-3095**	**3480-3482**	**3675-3677**	**3684-3686**	**3699-3701**	**3753-3755**	**3909-3911**	**4062-4064**	**4449-4451**	**4476-4478**	**4488-4490**
Codon observed	**AAA (Lys) AGA (Arg)**	**ATG (Met) TTG (Leu)**	**AAA (Lys) AAC (Asn) AAT (Asn)**	**ATT (Ile) ACT (Thr)**	**GUA (Val) GCA (Ala)**	**GTA (Val) ATA (Ile)**	**TCT (Ser) GCT (Ala)**	**GCT (Ala) GGT (Gly)**	**GAT (Asp) TAT (Tyr)**	**GAC (Asp) AAC (Asn)**	**AAT (Asn) GAT (Asp)**	**AAT (Asn) GAT (Asp) GAA (Glu)**	**GTA (Val) ATA (Ile)**	**AAT (Asn) AGT (Ser)**	**GCT (Ala) GGT (Gly)**
CPV-2	Arg	Met	Asn	Ile	Ala	Ile	Ser	Ala	Asp	Asn	Asn	Asn	Val	Ser	Gly
CPV-2a	Arg	Leu	Asn	Thr	Ala	Ile	Ser	Gly	Tyr	Asn	Asp	Asn	Ile	Ser	Gly
CPV-2b	Arg	Leu	Asn	Thr	Ala	Ile	Ser	Gly	Tyr	Asn	Asp	Asp	Val	Ser	Gly
New CPV-2a	Arg	Leu	Asn	Thr	Ala	Ile	Ala	Gly	Tyr	Asn	Asp	Asn	Val	Ser	Gly
New CPV-2b	Arg	Leu	Asn	Thr	Ala	Ile	Ala	Gly	Tyr	Asn	Asp	Asp	Val	Ser	Gly
CPV-2c	Arg	Leu	Asn	Thr	Ala	Ile	Ala	Gly	Tyr	Asn	Asp	Glu	Val	Ser	Gly

Figure 1. Amino acid variations in VP2 protein of CPV (Decaro & Buonavoglia, 2012)

Historical Perspective of CPV-2

A history of CPV-2 and its variants will be discussed along with the people involved in CPV-2's discovery & evolution throughout time. It is not possible to acknowledge all of the people involved in the research of the virus since its discovery 45 years ago in the summer of 1978, but the most significant individuals will be discussed. The pathology, pathogenesis, immune response, host range, diagnosis and vaccination of CPV-2 are well described in the literature. In more detailed studies, the properties & characteristics of CPV-2 & its variants are also well described. Drs. L. Carmichael & M. Appel of The Baker Institute were described as first isolating the virus in 1978 in the United States, but the virus was recognised in Europe & Australia around the same time. Between 1974 & 1976 in Belgium & Greece, dog sera were tested for the presence of antibodies & were shown to be positive (Schwers, et al., 1979) (Koptopoulos, et al., 1986). Schwers et al., showed in 1979 that CPV-2 was present in Europe in 1976 but in 1986, Koptopoulos, et al., reported that antibodies which inhibited haemagglutination & shown to neutralise CPV-2 were found in serum samples from Greek dogs in 1974 but the authors claimed that the results were non-specific & could have been due to an infection with a related parvovirus. It is thought the virus is a mutation of the Feline Panleukopaenia virus. The pathogenesis was determined between 1979-1983 by Carpenter et al., 1980, Robinson et al., 1980, Pollock, 1982, Macartney et al., 1984, Carman & Povey, 1985, Meunier et al., 1985. Immune response to field CPV-2 & candidate vaccines was described by Chappuis & Duret, 1980; Pollock & Carmichael, 1982, & Carmichael et al. 1983 (Carmichael, 2005).

The initial cases of the virus were characterised by haemorrhagic diarrhoea & myocarditis. By 1980, CPV-2 had been shown to have spread worldwide. This was due to movements of dogs, their owners & infectious faecal material on fomites by various means of transport. The conditions met by the virus during this time would not have made a difference to its transmission as the virus is very resistant to a plethora of conditions. Before the nature of the disease was determined, The Baker Institute received thousands of phone calls from veterinary surgeons & dog owners. At the same time, the media were reporting about various outbreaks and in some sense created pandemonium and accelerated the manufacture of myths surrounding the virus (Carmichael, 2005).

As the virus spread amongst the canine population throughout the world, it was shown that CPV-2 & FPV had a close relationship. This allowed for the deployment of heterologous vaccines, these were not seen to give reliable protection to puppies, possibly due to interference with MDA. There was variation seen in the effectiveness of using commercial FPV vaccines by Pollock & Carmichael in 1983. Unfortunately, inactivated vaccines, although effective, did not prevent virus transmission which led to the use of attenuated FPV vaccines being used in dogs. This was met with opposition from individuals for several reasons. Firstly, attenuated vaccines were seen as "dangerous". Secondly, it was suggested that CPV-2 evolved from FPV vaccines, and the use of these vaccines would have further consequences in the future. Ultimately these apphrehensions made the development of safe effective vaccines more important. In 1998, Truyen et al., showed these ideas were merely myth as it was shown the virus did not originate from field or vaccine strains of FPV. As with any virus epidemic, there was a decrease in the number of CPV-2 cases. This was due to herd immunity as a consequence of natural infection and use of vaccines (Carmichael, 2005).

Between 1981-1982, veterinary surgeons in the United States began to report an increase in cases of CPV in unvaccinated as well as vaccinated dogs. The symptoms were seen to be more severe, with puppies presenting with symptoms of shock, with or without haemorrhagic diarrhoea. It was evident that the canine parvovirus they were treating was unlike previous cases. This virus was a variant of CPV-2 and was identified as CPV-2a in 1979 (Shackelton, et al., 2005). This variant was different to CPV-2 due to amino acid changes of VP2, a capsid protein. It was seen that this variant was able to infect cats and became the dominant strain of the virus (Truyen, et al., 1996a). In 1984, another variant CPV-2b (VP2 426Asp) was discovered which differed due to a nucleotide substitution (Parrish, et al., 1991b). These

variants became the dominating viruses in the field, causing CPV-2 to disappear from the population in 1981 (Carmichael, 2005).

According to research conducted by Shackelton, et al., 2005 CPV-2 had already developed its first variant, CPV-2a, in 1976. It was also said as part of the study that the ancestral canine parvovirus first emerged 10 years prior to its first description. Interestingly, the authors made an observation concerning the evolutionary rate of the virus, specifically the rate of nucleotide substitution (Carmichael, 2005). This behaviour was more common in RNA viruses and that the emergent branch which separates FPV from CPV had a rate of substitution similar to that observed in RNA viruses such as HIV-1 (Jenkins, et al., 2002) (Drummond, et al., 2003).

In 2000, a new variant of CPV-2 was isolated. This variant was initially characterised as CPV-2b through PCR & antigenic analysis, but when the sequence of the capsid protein encoding gene was analysed it was shown that there was a change in the amino acid in an epitope of the capsid (Buonavoglia, et al., 2001). This variant became known as CPV-2c (VP2 426Glu) and according to Decaro, et al., CPV-2c had been detected in archived samples which had been collected in 1996 showing it had been in circulation in Europe since that time and possibly before 1996 before its official report. It is suggested that this variant is more sinister than the other variants in regard to the adult dog population (Decaro, et al., 2008). Conflicting findings suggest that this variant is less sinister than the other variants (Decaro, et al., 2005). According to MSD Animal Health, a fourth variant CPV-2d has emerged in some countries but there is no studies or literature as of yet to suggest that this variant is in circulation with the majority focusing on the three variants mentioned previously (MSD Animal Health, 2023). Recent outbreaks in Colorado in the United States has sparked the interest of Prof. Colin Parrish of The Baker Institute and a veterinarian Dr. Lindsey Dunn fears she may be dealing with a new strain of the virus but this remains to be speculation (Fiala, 2022). As seen in the literature the virus is capable of mutating and other variants of CPV-2 could reveal itself in years to come as according to Shackelton et al., the DNA virus has a high mutation rate with a rate of approximately 10^{-4} per site per year in a major capsid gene of the virus.

Prevalence & Distribution of CPV-2 in Europe

Despite vaccination protocols, CPV-2 still remains a prevalent cause of haemorrhagic enteritis in dogs especially puppies under the age of six months who are unvaccinated or partially vaccinated. Two studies conducted by Decaro et al. in 2007 & 2009 sought to study the distribution of CPV variants within Europe. In 2007 & 2009, 232 & 156 faecal samples respectively of CPV isolates were collected from dogs that were suffering from diarrhoea from 10 different countries. The countries from which the samples were obtained were Italy, Germany, The United Kingdom (UK), Portugal, Belgium, Spain, Switzerland, France, The Netherlands & Czech Republic. The German samples consisted of cell-culture adapted CPV strains which had been isolated from dogs with diarrhoea from 1996-2005. The samples were tested using polymerase chain reaction (PCR) technology & genetic variants were distinguished using minor groove binder probe assays (Ntafis, et al., 2010). In Italy the most common variant of CPV was CPV-2c from which it was first identified in 2000. In Germany & Portugal the most common variant is CPV-2b but CPV-2c is closely following behind. The UK only presented one sample testing positive for CPV-2c with the most common variant being CPV-2b. In Portugal & Spain, CPV-2a was not detected, but CPV-2c was shown to be present in both countries. In the Czech Republic, Switzerland & Belgium all samples were of the variant CPV-2a. Some samples from Italy & the UK were positive for the CPV-2 variant but this was due to these subjects being vaccinated shortly beforehand.

A study was conducted by Davies in 2008 in the UK with the aim to identify the strains of CPV-2 affecting the dog population. 106 samples were submitted as part of the study. 103 samples (97%) tested positive for the virus through PCR testing. Of the 103 samples, 34 (33%) tested positive for CPV-2a & the majority of samples tested positive for CPV-2b, with 69 (67%) positive samples. In this study CPV-2c was not isolated (Davies, 2008).

In a study conducted by Ntafis, et al., from March 2008 to March 2009, 167 faecal samples were collected from dogs suffering from diarrhoea from different regions in Greece. Of the 167 faecal samples, 84 were positive for CPV-2 (50.3%), the most common variant being CPV-2a with a total of 81 positive samples & the least common variant CPV-2b with one positive sample, CPV-2c was shown to be present in Greece with two samples testing positive.

In 2009 a study was undertaken by McElligot, et al., 2011 to determine the epidemiology of CPV-2 & its variants in Ireland. During the study, 250 faecal samples were submitted from asymptomatic and symptomatic patients from which 7 were positive for CPV-2. The testing

was conducted using PCR technology. Of the seven positive samples, three were revealed to be CPV-2a & four were revealed to be CPV-2b. CPV-2c has not been recorded in Ireland as of yet (McElligot, et al., 2011). In future research this may change as CPV-2c is spreading throughout Europe and through the importation of dogs such as the case seen in Italy from Thailand in 2017. Other than the study conducted in 2011, Ireland lacks in updating epidemiological data concerning CPV-2 and its variants, this is detrimental to the canine population of Ireland.

In 2010, Filipov, et al., conducted research into the epidemiology of CPV-2 and its variants in Bulgaria. They collected 42 faecal samples from dogs with clinical signs of CPV. The samples were tested using antigen testing in rapid tests and PCR. The variants were detected using minor groove binder probe PCR assays. Of the 42 samples, 40 samples tested positive (95.23%) (Filipov, et al., 2011). 30 of the positive samples were identified as CPV-2a, nine were positive for CPV-2b, with the variant CPV-2c also present in the state.

In 2014, Cságola, et al., also conducted a study into identifying CPV-2 strains circulating in Hungary. According to the author, the number of infections was increasing amongst vaccinated dogs which sparked the interest in the study. 50 samples were submitted with 42 testing positive for CPV-2 (84%) using PCR technology.

An imported case of parvovirus was detected in Italy from Thailand in 2017 (Mira, et al., 2017). The four-month-old Pomeranian showed typical clinical signs of parvovirosis two days after it had been imported to Italy. The dog died despite efforts to treat the disease & the body was subjected to a necropsy in which all tissues tested positive for CPV-2 using PCR technology. During sequence analysis it was shown the sample had aa changes that had not been observed in CPV-2 strains isolated in Europe and that was more closely related to the strains seen in Asia, confirming the strain had been imported from Thailand. According to the authors, there was changes affecting the NS1 sequence which were observed in strains isolated in China between 2013-2014. The infection was found to have to be caused by CPV-2c (Mira, et al., 2017).

Following on from the case in Italy, an article submitted by Boros et al in 2022 investigated an outbreak of haemorrhagic gastroenteritis in a colony of Jack Russell Terriers (JRT) in Hungary which were vaccinated against the disease. A rectal sample from a seven-week-old puppy tested positive for CPV-2. The strain was shown to be different from strains used in vaccines & previously isolated strains in Hungary. The strain, FR1/CPV2-2021-HUN showed close sequence identity & phylogenetic relationship to the previously described CPV-2c strain

isolated from the imported case in Italy. Due to an amino acid difference on position 426 of VP2, the mentioned strain belonged to the CPV-2b antigenic variant (Boros, et al., 2022). The study involved puppies ranging from ages seven to eight weeks old with a mortality rate of approximately 60%. The puppies had received there first of their primary vaccinations at six weeks old and received their booster vaccination two to three weeks later. In this study, nine subjects tested positive for the virus, some of which did not test positive on a rectal swab but during testing of the organs such as the lymph nodes, spleen & thymus (Boros, et al., 2022).

In 2022, Milicevic et al. conducted a study into CPV-2 & its variants in Serbia. They collected 50 rectal swab samples from 2008 to 2020. It was concluded from the study that the most prevalent variant was CPV-2a (60%) and in 2020 the first detection of CPV-2c occurred but it is likely that the variant was in circulation before this detection.

Control Measures

Vaccination Programs

Vaccination is considered the most important form of disease prevention. It also prevents the large cost of treatment if a dog falls ill with CPV as well as the emotional toll it takes on both the owners & veterinary professionals alike. This disease is preventable & clients must be educated on the importance of vaccination. Without vaccination the disease will make a resurgence in Europe, with much higher rates of incidence than can be seen today. Ideally, canine parvovirus vaccination would ultimately eradicate the virus & its variants but due to immunisation failures this is not realistic. The most important immunisation failures include the interference of maternally derived antibodies, non-responders & the possibility of reversion to virulence (Decaro, et al., 2020). The vaccine is viewed by the WSAVA to be a core vaccine, meaning it is a vaccine that should be administered to all dogs, at recommended intervals, to provide life-long protection against significant diseases (Day, et al., 2016). The listed core vaccines protect against CPV-2, Canine Adenovirus types 1 & 2 & Canine Distemper Virus. Some countries may require other vaccines to be a core vaccine such as the Rabies vaccine. According to Day, et al., 2016 it is not recommended to vaccinate puppies less than 6 weeks old or pregnant dams due to adverse effects such as foetal damage.

The most widely used parvovirus vaccine in use today is the modified live virus vaccine. These vaccines induce strong immunity as the virus can replicate in the host's body without causing disease. The strains of the virus used in this vaccine are CPV-2, CPV-2a & CPV-2b but not all vaccines contain all 3 strains as seen in Versican Plus DHPPi which contains only

CPV-2b. Nobivac® Parvo-C contains all three of the above variants. These vaccine strains can cause a viraemia and elicit an immune response. They replicate in the intestinal mucosa which leads to the vaccine virus being shed in faeces. A study by Freisl, et al., 2017 was carried out to assess faecal shedding of CPV after modified live virus vaccination. It showed that out of 100 dogs, 23% shed CPV from day three to day 28 post-vaccination. (Freisl, et al., 2017) This may lead to a dog having a false positive test result if presented to a clinic with diarrhoea.

MLV vaccines have a long duration of immunity with studies showing protection of dogs three days post vaccination (Schultz & Larson, 1996). Even though yearly boosters are recommended, studies have shown up to nine years of protection post vaccination. (Schultz, et al., 2010) Examples of modified live vaccines used in the European market are Versican Plus DHPPi, Nobivac® DHPPi & Nobivac® Parvo-C. Versican Plus DHPPi is composed of live attenuated viruses to protect against Canine Distemper Virus, strain CDV Bio 11/A, Canine Adenovirus type 2, strain CAV-2 Bio 13, CPV-2b, strain CPV-2b Bio 12/B & Canine Parainfluenza type 2 virus, strain CPiV-2 Bio 15. The vaccine can be used in puppies from the age of six weeks with onset of immunity three weeks after the first vaccination. The second vaccination can be administered three to four weeks later. According to the manufacturer, duration of immunity is expected to be at least three years post administration of the primary course of vaccination. It was shown that the shedding of the vaccine virus occurs up to 10 days post vaccination. According to the manufacturer the vaccine is safe to use in dams in the second & third trimester of gestation (European Medicines Agency, 2019). Nobivac® DHPPi acts in the same fashion as the previous product with some variation. Puppies can be vaccinated from six weeks of age with onset of immunity one week after the first vaccination. The second vaccination can be administered two to four weeks later once the second dose is administered when the puppy is 10 weeks of age or older. As seen in the previous product, immunity is expected to last at least three years with booster vaccination recommended every three years. The manufacturer states the vaccine is safe for use during gestation (Health Products Regulatory Authority, 2021). Nobivac® Parvo-C is also composed of a live attenuated virus but differs to the previous product as its sole purpose is to vaccinate against canine parvovirus and its variants. The product contains CPV strain 154. Puppies can be vaccinated from six weeks of age, but it is recommended by the manufacturer to administer the product at 10 weeks of age due to the interaction with MDA. The vaccine protects the dog for up to three years with a booster vaccine to be administered every 3 years. According to the manufacturer the product can be used during gestation if the dam has previously been vaccinated with CPV strain 154 antigens before (Health Products Regulatory Authority,

2021). There are few inactivated CPV vaccines available, but these vaccines have been shown to have low immunogenicity (Decaro, et al., 2020).

Age at presentation	Vaccination Schedule
6 weeks	6 weeks, 9 weeks, 12 weeks, 16 weeks then 26 or 52 weeks or 6 weeks, 10 weeks, 14 weeks, 18 weeks then 26 or 52 weeks
7 weeks	7 weeks, 10 weeks, 13 weeks, 16 weeks then 26 or 52 weeks or 7 weeks, 11 weeks, 15 weeks, 19 weeks then 26 or 52 weeks
8 weeks	8 weeks, 11 weeks, 14 weeks, 17 weeks then 26 or 52 weeks or 8 weeks, 12 weeks, 16 weeks then 26 or 52 weeks
9 weeks	9 weeks, 12 weeks, 15 weeks, 26 or 52 weeks or 9 weeks, 13 weeks, 17 weeks then 26 or 52 weeks
Adult	2 doses 2 – 4 weeks apart but one dose of MLV vaccine is considered protective
Booster vaccination	Revaccinate at 6 months or 12 months of age, then not more than every 3 years

Figure 2. WSAVA Canine Vaccination Guidelines (Day, et al., 2016)

Initial vaccine series for puppies	Initial vaccine series for adults
Administer first dose on admission to puppies as early as 4 weeks old, repeat at 2-week intervals until 20 weeks old if animal remains at the facility	Administer first dose on admission, repeat in 2 weeks.

Figure 3. WSAVA Guidelines on canine vaccination for the shelter environment (Day, et al., 2016)

Hygiene & Sanitisation

As CPV-2 can withstand a multitude of conditions it must be removed artificially by removing faecal material from the environment and placing it in clinical waste & the area disinfected with suitable disinfectants. Fomites such as blankets and bedding must be laundered in a suitable disinfectant at high temperature or disposed of in clinical waste. Surfaces such as those with porous surfaces or scratched surfaces are more difficult to clean as the virus can remain in these crevices, making it more difficult to disinfect. Luckily there are products available on the market which can be used in disinfection. Disinfection is a process whereby the number of microorganisms is decreased to a level where they are no longer a threat to an animal's health. There are a number of factors to consider when choosing a disinfectant; contact time, corrosive effects, toxicity, spectrum of activity & intended use (Monsey & Devaney, 2011).

Sodium hypochlorite, a halogen, or more commonly known as bleach can be used in the disinfection of CPV-2 but it can be harsh on surfaces, especially fabric & wood. The major disadvantage of bleach is that it is inactivated by organic material such as faeces, which is the source of infection. In an in vitro study, it was shown that a concentration of 0.75% with a contact time of one minute can reduce the amount of virus on surfaces. According to the WOAH it is recommended to disinfect with 2% sodium hypochlorite solution. (World Organisation for Animal Health, 2021) It is important to acknowledge that this disinfectant can be irritating to body surfaces and eyes & must not be significantly overdosed which can also be uneconomical (Cavalli, et al., 2018).

Potassium peroxymonosulphate (Virkon® S), an oxidising agent, can be used in the disinfection of CPV-2. Its activity is reduced in the presence of organic material, it is also corrosive to metal surfaces. The method by which it works is through the breaking down of proteins, deactivating the virus. According to the manufacturer, a 1% solution is recommended to disinfect surfaces. Metal food and water bowls can be soaked in a 1% solution for up to 10 minutes and rinsed (Lanxess, 2018). It is recommended to allow a contact time of 1 hour on other surfaces (The University of Nottingham, 2012). As before, if under diluted the product can be irritant to skin and eyes.

Halogenated tertiary amine compounds (Distel), can be used in the disinfection of CPV. It is recommended to use a 2% solution (The University of Nottingham, 2012).

Aldehydes such as formaldehyde can be used to disinfect canine parvovirus but due to its hazardous characteristics i.e. carcinogenic, it is recommended to use other materials such as those mentioned previously.

A strict cleaning protocol must be implemented. Organic material should be removed and disposed of correctly. A disinfectant applied and given the correct contact time.

Biosecurity Measures

Biosecurity plays a significant role in the control of infectious agents such as CPV and must not be underestimated. Its purpose is to protect personnel & clients, protect patients from nosocomial infection, break the transmission cycle & ensure the correct cleaning & disinfection protocols are implemented. Canine parvovirus does not pose a risk to humans, but clients & personnel can carry the virus into or out of the facility via fomites, spreading the virus to vulnerable puppies & adult dogs. Measures such as isolation facilities, barrier nursing, personal protective equipment (PPE), hand hygiene, disinfection protocols and

correct disposal of infectious material must be employed in practice to ensure the success of biosecurity & reviewed accordingly (Monsey & Devaney, 2011).

- PPE: Staff should wear all PPE provided including separate scrubs, plastic aprons, and latex/ nitrile gloves & shoe covers. Ideally the facility would also provide separate footwear.
- Hand hygiene: Before entering & leaving the isolation facility it is vital to ensure correct hand cleaning procedures are used by providing hand washing facilities. Hands should be washed with soap & water & an alcohol-based rub used after. Hands must be washed between patients, prior to donning gloves & after their removal.
- Isolation: The room or facility in which the patient is being treated must contain all equipment & medication necessary to provide optimum treatment the patient. The facility or room should ideally contain its own water source, laundering equipment, bathing facilities & waste bins i.e. clinical waste. Any equipment used in isolation must be kept within the room or facility unless appropriately disinfected or sterilised.
- Barrier nursing: Nursing & veterinarians must use the appropriate PPE and keep contact with the patient to a minimum when administering treatment and cleaning and disinfecting kennels.
- Clinical waste: All soiled materials should be placed in a yellow clinical waste bin that is labelled appropriately.
- Disinfection protocol: Cleaning & disinfection must be carried after the departure of each patient from the facility & the correct disinfectant such as those mentioned must be used & the appropriate contact time allowed. Bedding & scrubs must be laundered separately from general laundry at a high temperature (>60^{o}C) with an appropriate detergent and disinfectant. It is advisable to bath dogs after successful treatment to remove any traces of the virus.

Quarantine & Isolation Protocols

When a puppy or adult dog presents to the clinic with symptoms of CPV-2 it is important to suspect canine parvovirosis as part of your differential diagnosis. Thorough history should be taken, clinical exam conducted, & vaccination history noted. If the animal has not been vaccinated, has not completed the primary course of vaccination, or has not received a booster vaccine within the last three years, it is advised to test for canine parvovirus. If the dog tests positive for CPV-2, it is essential to isolate the patient. It is recommended that the length of isolation is 14 days. After isolation it is advised to quarantine your puppy or dog for a further 14 days post-recovery as viral shedding can still occur (University of California Davis, 2017).

Method

In this literature review, Google Scholar was used to search for journal articles about CPV, its variants, their distribution in Europe, breeds affected and variation in clinical signs of CPV, but also Elsevier, Science Direct & PubMed were utilised. In addition to references from the web, a book was used to gather information on barrier nursing and isolation protocol from the textbook BSAVA Textbook of Veterinary Nursing 5th edition (Monsey & Devaney, 2011).

Search words used for this paper included the following: Canine parvovirus, variants of canine parvovirus, CPV-2a, CPV-2b, CPV-2c, canine parvovirus history, vaccination, breeds, clinical signs, CPV-2 in Europe, vaccination failures, isolation, biosecurity.

Journal articles from Europe were used which studied groups of animals or samples from CPV-2 affected animals. CPV-2 was detected using ELISA & PCR. PCR is considered more accurate, giving more reliable results.

It was found to be important to focus on research from the last five years but as there was a lack of research on CPV-2 in Europe during that time earlier papers from 2007-2022 were also utilised for this literature review.

This paper summarises the distribution of CPV-2 and its variants in Europe, control programs, breeds affected & variation in clinical symptoms.

Results

From 2007 – 2022, 464 dogs, with their gender disclosed, tested positive for CPV-2 from five different countries in Europe. Namely, Hungary, Portugal, Greece, Poland & Slovenia. The data was obtained using the following studies:

(Boros, et al., 2022) (Miranda, et al., 2015) (Kalli, et al., 2010) (Kantere, et al., 2021) (Wójcik, et al., 2021) (Gombac, et al., 2008)

Hungary: Among the 10 cases, six were male and four were female.

Portugal: Among the 162 cases, 93 were male and 69 were female.

Greece: Among the 162 cases, 101 were male and 61 were female.

Poland: Among the 46 cases, 26 were male and 20 were female.

Slovenia: Among the 84 cases, 70 were male and 14 were female.

In total there was 296 (63.79%) male cases and 168 (36.21%) female cases as can be visualised in figure 4.

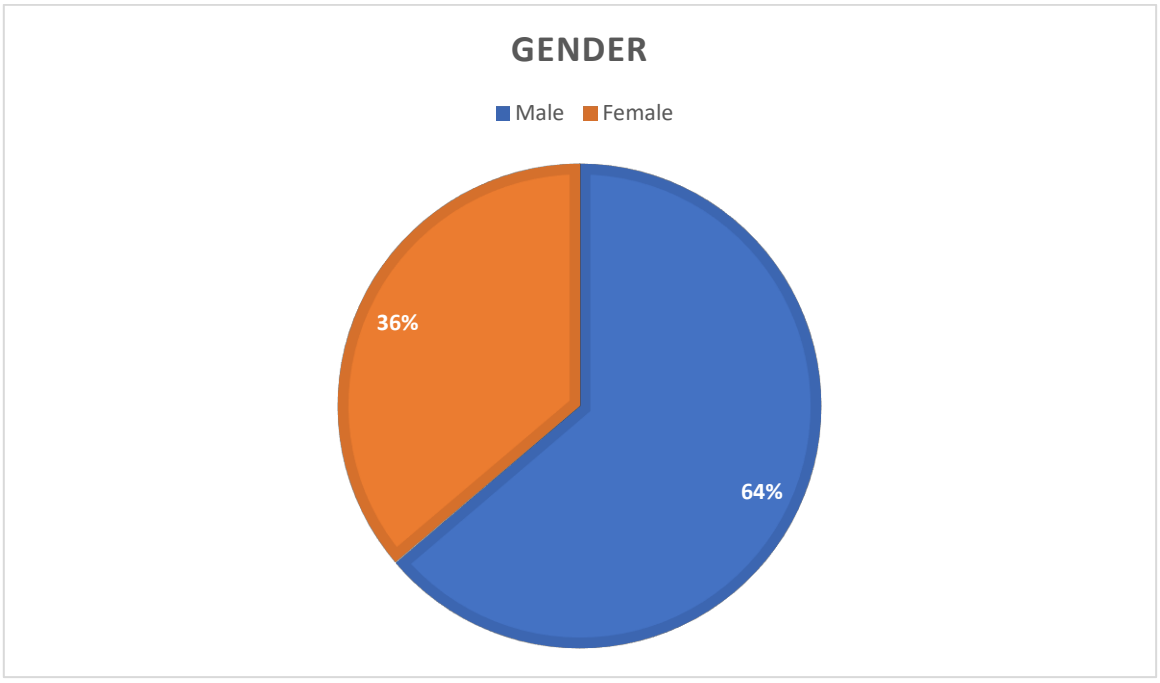

Figure 4. Gender distribution of CPV

In total, 1,028 dogs were assessed from 2007-2022 in the literature reviewed. Not all studies provided the breed of all patients, with a total of 670 (65.18%) patients without breed specification. A total of 14 studies examining 16 different countries in Europe were used to compile this data. The countries included are: The UK, Greece, Italy, Hungary, Bulgaria, Ireland, Serbia, Poland, Portugal, Slovenia, Spain, Belgium, Czech Republic, Switzerland,

France & Germany. Different sized dogs were affected by CPV-2 with the largest affected population being crossbreeds, representing 19.26% of the studied population. The German Shepherd Dog represented 3.4%. The Rottweiler represented 2.14% of the population. The Labrador retriever represented 1.5% of the population. The Jack Russell terrier & the Poodle represented 0.97% of the population each. The Collie represented 0.68% of the studied population. The Cocker Spaniel represented 0.58% of the population. The Chihuahua represented 0.49% of the population. The Spitz represented 0.39% of the sample. The Cavalier King Charles Spaniel, Lurcher, White Swiss Shepherd, Maltese and Pit Bull terrier all represented 0.29% each. The Golden Retriever, English Setter & German Short-haired Pointer all represented 0.19% each. Other breeds such as the Pomeranian, Yorkshire terrier, Bulgarian Shepherd Dog, Akita, Central Asian Shepherd Dog, Sheepdog, Spaniel, Czechoslovakian Wolfdog, Welsh terrier, Dobermann Pinscher, Great Dane, Brittany, English Pointer, Caucasian Shepherd Dog, French Pointer & Dalmatian were each represented in one individual case, constituting 0.1% of the sample each. These figures can be seen in figure 5. The data was obtained from the following studies: (Davies, 2008) (Ntafis, et al., 2010) (Mira, et al., 2017) (Boros, et al., 2022) (Ságola, et al., 2014) (Filipov, et al., 2011) (McElligot, et al., 2011) (Milicevic, et al., 2023) (Kantere, et al., 2021) (Wójcik, et al., 2021) (Kalli, et al., 2010) (Miranda, et al., 2015) (Gombac, et al., 2008) (Decaro, et al., 2007) (Decaro, et al., 2011)

Breed	Count	Percentage
Total	1028	
Not Specified	670	65.18%
Crossbreed	198	19.26%
German Shepherd Dog	35	3.4%
Rottweiler	22	2.14%
Labrador Retriever	16	1.5%
Jack Russell Terrier	10	0.97%
Staffordshire Bull Terrier	9	0.88%
Poodle	9	0.88%
Collie	7	0.68%
Cocker Spaniel	6	0.58%
Chihuahua	5	0.49%
Spitz	4	0.39%
Cavalier King Charles Spaniel	3	0.29%
Lurcher	3	0.29%
White Swiss Shepherd	3	0.29%
Maltese	3	0.29%
Pit Bull Terrier	3	0.29%
Golden Retriever	2	0.19%
English Setter	2	0.19%
German Short-haired Pointer	2	0.19%
Pomeranian	1	0.1%
Yorkshire Terrier	1	0.1%
Bulgarian Shepherd Dog	1	0.1%
Akita	1	0.1%
Central Asian Shepherd Dog	1	0.1%
Sheepdog	1	0.1%
Spaniel	1	0.1%
Czechoslovakian Wolfdog	1	0.1%
Welsh Terrier	1	0.1%
Dobermann Pinscher	1	0.1%
Great Dane	1	0.1%
Brittany	1	0.1%
English Pointer	1	0.1%
Caucasian Shepherd Dog	1	0.1%
French Pointer	1	0.1%
Dalmatian	1	0.1%

Figure 5 Breed Distribution of CPV

From the data gathered from 15 countries from the literature from 2007 – 2022, presented under the heading “Prevalence & Distribution of CPV-2 in Europe” it can be seen that CPV, and its variants are ever present in Europe with a variant of the virus being discovered in Italy in 2000 with evidence of the virus in circulation in Germany before this. Of the samples, 645 were determined to be either CPV-2a, CPV-2b or CPV-2c. From the literature The UK presented the most cases of CPV-2 in Europe with a total of 150 cases (23.26%), with Italy right behind with 125 cases (19.38%). Greece presented 84 (13.02%) cases of CPV-2 making it the third highest in Europe for CPV-2. Germany presented 52 (8.06%) cases of CPV-2 with Hungary closely following behind with 51 cases (7.91%). Poland presented 46 cases (7.13%)

of CPV-2 followed by Bulgaria with 40 cases (6.2%). Portugal was eighth on the list with 31 cases (4.8%) of CPV-2, followed by Belgium & Spain with 17 (2.64%) & 14 (2.17%) respectively. Both France & Serbia presented 13 cases (2.02%) each. Ireland presented 7 cases from a study conducted in the south of the country by McElligot, et al., 2011 making up 1.09% of cases. The Czech Republic and Switzerland both presented a singular case each representing 0.16% of cases each. The most cases occurred in the UK whilst the least cases occurred in the Czech Republic & Switzerland. The data was obtained from the following studies: (Decaro, et al., 2007) (Decaro, et al., 2011) (Davies, 2008) (Boros, et al., 2022) (Cságola, et al., 2014) (Filipov, et al., 2011) (Gombac, et al., 2008) (Kalli, et al., 2010) (Kantere, et al., 2021) (McElligot, et al., 2011) (Milicevic, et al., 2023) (Mira, et al., 2017) (Miranda, et al., 2015) (Schwers, et al., 1979) (Shackelton, et al., 2005) (Wójcik, et al., 2021)

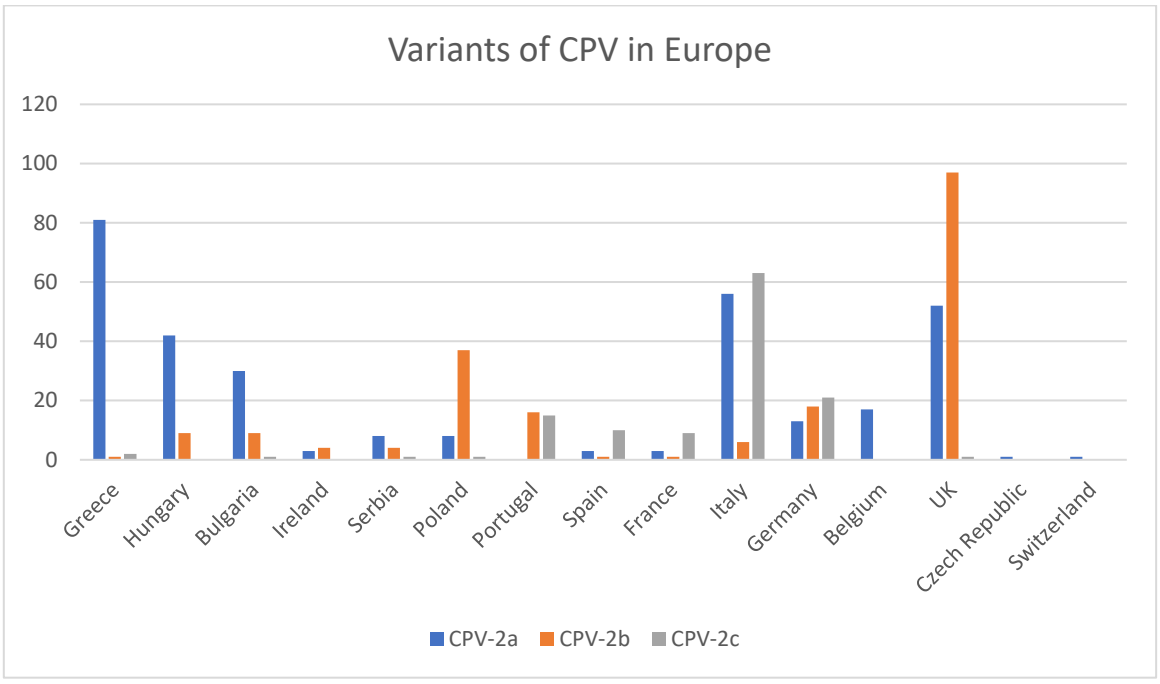

Figure 6 CPV Variant distribution in Europe

The first of the CPV variants in Europe is CPV-2a. It is the most prevalent variant in Europe. It is the oldest of the variants & from the literature can be seen to be present in 14 out of the 15 countries from which literature was published. In total there was 318 cases of CPV-2a published in the reviewed literature. It has the highest prevalence in Greece with a figure of 81 cases (25.47%) representing over a quarter of cases. Italy has the second highest prevalence of CPV-2a with 56 cases (17.61%) closely followed by the UK with 52 cases (16.35%). Hungary presented 42 cases (13.21%) of CPV-2a with Bulgaria presenting 30 cases (9.43%). Belgium presented 17 cases (5.35%) followed by Germany with 13 cases (4.09%).

Both Serbia & Poland presented 8 cases (2.52%) each. Ireland, Spain & France presented 3 cases each (0.94%) with Czech Republic & Switzerland presenting a singular case each (0.31%). Interestingly, Portugal did not show the presence of CPV-2a. This data can be seen in a geographic distribution map of Europe in figure 7. The data was obtained from the following studies: (Decaro, et al., 2007) (Decaro, et al., 2011) (Davies, 2008) (Boros, et al., 2022) (Cságola, et al., 2014) (Filipov, et al., 2011) (Gombac, et al., 2008) (Kalli, et al., 2010) (Kantere, et al., 2021) (McElligot, et al., 2011) (Milicevic, et al., 2023) (Mira, et al., 2017) (Miranda, et al., 2015) (Schwers, et al., 1979) (Shackelton, et al., 2005) (Wójcik, et al., 2021)

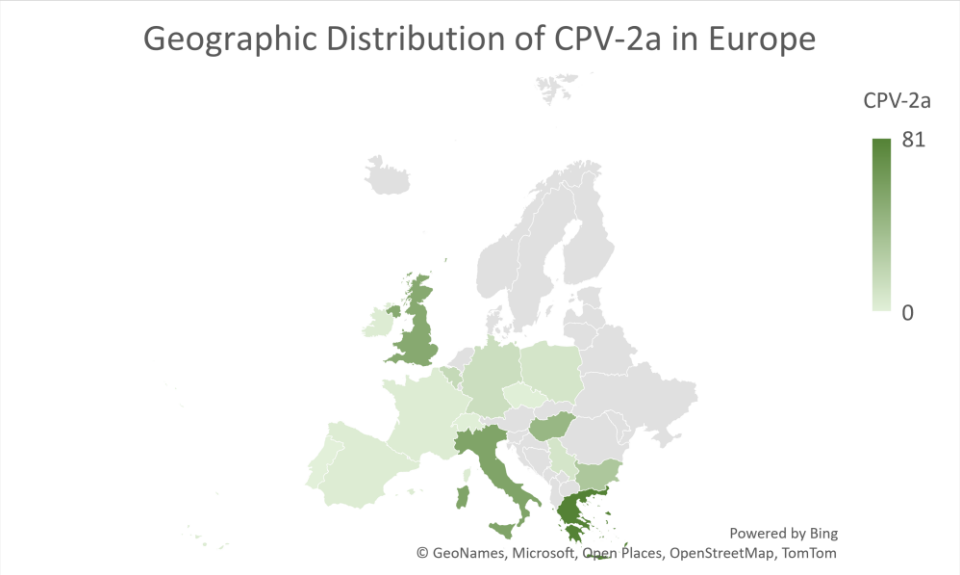

Figure 7. Geographic Distribution of CPV-2a in Europe

The second of the CPV variants in Europe is CPV-2b. It is the second most prevalent variant in Europe. It is the second oldest of the variants & from the literature can be seen to be present in 12 out of the 15 countries from which literature was published. In total there was 203 cases of CPV-2b published in the reviewed literature. It has the highest prevalence in the UK with 97 cases (47.78%), representing almost half of cases. Poland has the second highest prevalence of CPV-2b in Europe with a total of 37 cases (18.23%) followed by Germany with 18 cases (8.87%). Portugal has the fourth highest prevalence of CPV-2b with 16 cases (7.88%) followed by Bulgaria & Hungary with nine cases each (4.43%). Ireland & Serbia both presented 4 cases each (1.97%). Greece, Spain & France only reported a single case each (0.49%). Interestingly, Czech Republic, Belgium & Switzerland did not report a case of CPV-2b. This data can be seen in a geographic distribution map of Europe in figure 8. The data was obtained from the following studies: (Decaro, et al., 2007) (Decaro, et al., 2011)

(Davies, 2008) (Boros, et al., 2022) (Cságola, et al., 2014) (Filipov, et al., 2011) (Gombac, et al., 2008) (Kalli, et al., 2010) (Kantere, et al., 2021) (McElligot, et al., 2011) (Milicevic, et al., 2023) (Mira, et al., 2017) (Miranda, et al., 2015) (Schwers, et al., 1979) (Shackelton, et al., 2005) (Wójcik, et al., 2021)

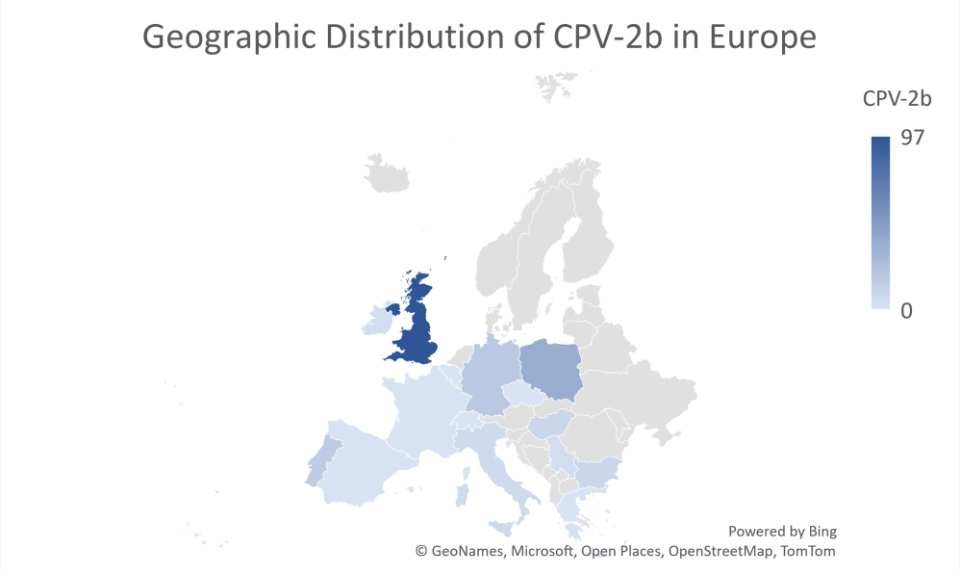

Figure 8. Geographic Distribution of CPV-2b in Europe

The third of the CPV variants in Europe is CPV-2c. It is the third most prevalent variant in Europe. It is the third oldest of the variants & from the literature can be seen to be present in nine out of the 15 countries from which literature was published. In total there was 124 cases of CPV-2c published in the reviewed literature. It has the highest prevalence in Italy where it was first described in 2000, with 63 cases (50.81%), making up over half of cases in Europe. The country with the second highest amount of CPV-2c cases is Germany from where there is a history of the virus prior to its first description in 2000 in Italy. Here there was seen to be 21 cases (16.94%). The third highest was Portugal with 15 cases representing 12.1% of cases. Spain was seen to have 10 cases (8.06%) followed directly by France with nine cases (7.26%) Greece was found to have quite a low amount of CPV-2c compared to the amount of CPV-2a cases with two cases (0.93%). Lastly, Bulgaria & the UK were found to only report a single CPV-2c case each (0.47%). Interestingly, Hungary, Ireland, Belgium, Czech Republic & Switzerland have not officially reported a case of CPV-2c during the writing of this literature review. This data can be seen in a geographic distribution map of Europe in figure 9. The data was obtained from the following studies: (Decaro, et al., 2007) (Decaro, et al., 2011) (Davies, 2008) (Boros, et al., 2022) (Cságola, et al., 2014) (Filipov, et al., 2011) (Gombac, et al., 2008)

(Kalli, et al., 2010) (Kantere, et al., 2021) (McElligot, et al., 2011) (Milicevic, et al., 2023) (Mira, et al., 2017) (Miranda, et al., 2015) (Schwers, et al., 1979) (Shackelton, et al., 2005) (Wójcik, et al., 2021)

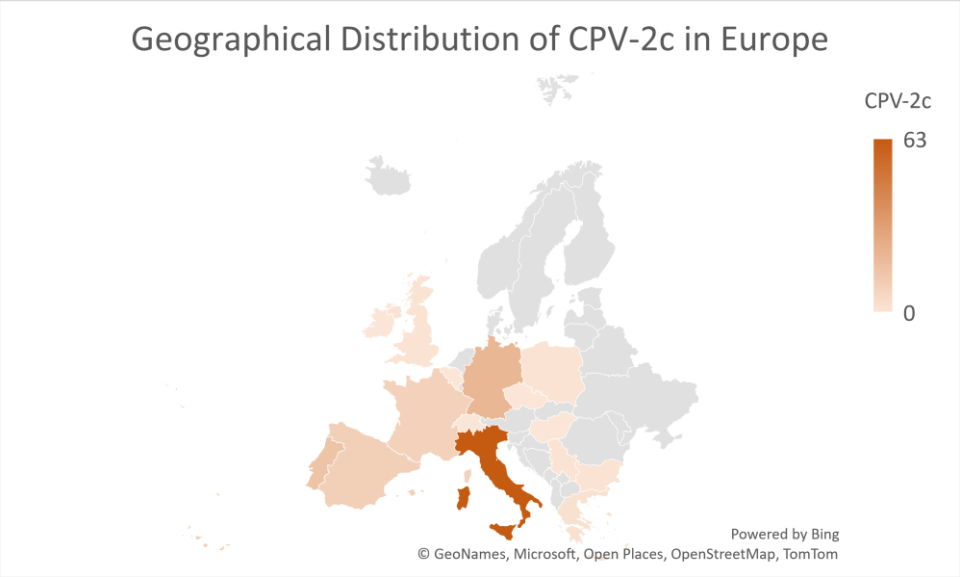

Figure 9. Geographical distribution of CPV-2c in Europe

In regard to clinical symptoms of the affected patients several patterns were observed. In total clinical signs were provided for 455 patients in nine different studies from eight different countries. Listed clinical signs in figure 10 come from Slovenia, Portugal, Greece, Poland, Serbia, Ireland, Hungary & one case from Italy. The most common clinical symptom described was diarrhoea, representing 89.89% representing a large number of cases. Similarly vomitus was highly prevalent, shown to affect 71.43% of cases. Thirdly, lethargy was also seen to affect a large number of cases, representing 68.13% of patients affected. Dehydration, ultimately due to anorexia, vomitus and diarrhoea was seen in 38.68% of cases. A cause of dehydration, anorexia represented 33.85% of symptoms in cases presented. Pale mucous membranes due to hypotension was seen in 20% of cases. Hand in hand, an increased capillary refill time due to dehydration and shock was seen in 6.81% of cases. Upon abdominal palpation, discomfort was shown to represent 4.84% due to the gastroenteritis. Hypothermia could also be seen in 2.42% of cases and from my own personal observation in affected puppies, hypoglycaemia can be seen which is detrimental to a young puppy's health as it can lead to seizures. Interestingly, it was described that a JRT died of canine parvovirus whilst asymptomatic (Boros, et al., 2022) The variation in clinical signs can be seen in figure 10. The data was obtained from the following studies: (Decaro, et al., 2007) (Decaro, et al.,

2011) (Davies, 2008) (Boros, et al., 2022) (Cságola, et al., 2014) (Filipov, et al., 2011) (Gombac, et al., 2008) (Kalli, et al., 2010) (Kantere, et al., 2021) (McElligot, et al., 2011) (Milicevic, et al., 2023) (Mira, et al., 2017) (Miranda, et al., 2015) (Schwers, et al., 1979) (Shackelton, et al., 2005) (Wójcik, et al., 2021) (Mylonakis, et al., 2016)

Clinical Symptom	Percentage
Diarrhoea (+/- Haemorrhagic)	89.89%
Vomitus	71.43%
Lethargy	68.13%
Dehydration	38.68%
Anorexia	33.85%
Pyrexia	30.55%
Pale mucous membranes	20%
Increased capillary refill time	6.81%
Abdominal pain	4.84%
Hypothermia	2.42%
Asymptomatic	0.23%

Figure 10 Clinical Signs of CPV in Patients

Figure 11. Haemorrhagic Diarrhoea seen in a Bulldog puppy (Richter, 2019)

Discussion

The preceding chapters of this thesis literature review have presented CPV-2 and its variants with focus on their distribution in European countries from a collection of literature published by various researchers from 2007-2022. The variations in clinical signs & control measures were also presented.

To understand CPV-2 & its variants it was important to bring attention to its history & evolution. The virus emerged in the late 1970s & in 45 years has shown its ability to mutate & potentially evade current vaccine antibodies. It was shown by Shackelton, et al., 2005, the DNA virus has a high mutation rate with a rate of approximately 10^{-4} per site per year in a major capsid gene of the virus. This mutation rate shows the importance in researchers & vaccine manufacturers remaining cautious & to conduct research into CPV-2 variants circulating in the population currently.

To this day despite vaccination protocols with MLV vaccines, CPV-2 remains a threat to the health of unvaccinated puppies & those who have not finished their primary core vaccinations. It was shown that CPV-2 has a morbidity rate of 100% & a mortality rate of 90% in untreated cases which can be reduced to under 20% when a patient receives the correct treatment. Since its first description in the late 70s it has mutated three times & some sources are mentioning a fourth variant, CPV-2d. It has killed a substantial number of puppies & dogs since its emergence and in that time created a significant impact on veterinary medicine. Not only has the virus had a fatal impact, it has had an emotional and economical impact as well. As the virus is more often seen in young puppies, emotions are more often than not an impactful side effect of the virus as young puppies pass away. This can impact the owners and breeders as well as veterinary personnel. The virus is unforgiving therefore a vaccine is required to aid in the immunisation of dogs around the globe. Unfortunately, vaccinations are not cheap & in order for your dog to have a fighting chance against this virus a vaccine is necessary. Due to some owner's economical background, vaccinations are not a priority, which predisposes their pet to infection.

From the literature reviewed, it was shown that certain breeds were shown to be more susceptible to the virus such as crossbreeds & German shepherd dogs with the rottweiler following behind. This may be an overrepresentation of certain breeds or may be due to economical background. It must also be appreciated that this sample of dog breeds may underrepresent the dog population in Europe. It was shown from the results that a larger dog is not more likely to become infected with CPV compared to small dog breeds as shown in

figure 5. In figure 4, 64% of presented cases were male with the remainder 36% representing female patients. This showed that males are more likely to be infected with CPV compared to females, but this may an over representation of the male dog population & an under representation of the dog population as a whole.

As seen in figure 10, clinical signs can vary between patients with not all patients experiencing the virus in the same way. It can be said that the worse the clinical signs become the poorer the prognosis of a case will be. The most common clinical signs of CPV-2 include diarrhoea, vomiting, lethargy, anorexia & dehydration. The most common, almost 90%, being diarrhoea which may or may not be haemorrhagic in nature. The least common clinical signs include pale mucous membranes, increased CRT, and hypothermia. Ultimately if these signs are seen it can be said the animal is in a deteriorating condition as they are hypovolaemic, showing signs of shock and not regulating their body temperature. Most importantly, young small breed puppies can experience hypoglycaemia which can lead to the occurrence of seizures, deteriorating the condition further. Early diagnosis can be obtained if the animal is known to have come in contact with a CPV-2 positive animal or shows early signs of infection such as lethargy, anorexia, and diarrhoea and/ or vomitus. It is of upmost importance to diagnose the clinical signs correctly as the patient will be treated symptomatically & parameters must be recorded & adjusted as required.

Thankfully at present time the virus can be controlled through the use of vaccination, enforcing biosecurity, & treating a patient in isolation. Puppies are ideally vaccinated at four to six weeks of age & then vaccinated every three to four weeks until 16 weeks old. Adult dogs should also receive core vaccinations if they have not already received them, it is important to record all vaccinations for future reference in case of occurrence of disease or to note the required timeline for a booster vaccination which is recommended to occur every three years. Vaccination is the best weapon against the virus and the prevention of the disease. MDA can interfere with the efficacy of vaccination but these decrease after eight to 12 weeks post-partum, from which time at least one more MLV vaccine will be administered. When socialising puppies outside the home it is recommended to only socialise with vaccinated dogs, but it is worth noting they can still carry the virus. Unfortunately, dogs still to this day fall ill with CPV and strict protocols must be followed in order to limit the spread of the virus which is highly transmissible & resistant in the environment. The patient must be isolated immediately after diagnosis to limit the spread of CPV and begin their treatment. Strict protocol must be followed by staff such as using PPE, barrier nursing and hand hygiene.

Biosecurity must not be neglected as the patient will produce highly infectious waste during their time in a veterinary facility. Waste must be placed in clinical waste & disposed of correctly, PPE must be worn correctly and disposed of after use. Biosecurity & isolation must be respected entirely as without these protocols, the virus can escape the facility, leading to a nosocomial infection to dogs e.g. puppies on their first appointment to a veterinarian for their first vaccinations.

CPV-2 and its variants are dispersed throughout Europe as seen in the referenced literature. Some countries have a higher percentage of CPV-2a or CPV-2b or CPV-2c. It has been mentioned there is a fourth variant in circulation. CPV-2a is the highest circulating variant in Greece whilst it is not shown to be in circulation in Portugal. CPV-2b is the highest circulating variant in the UK whilst it is not shown to occur in Switzerland or Czech Republic, CPV-2c is the highest circulating variant in Italy from where it was first described in 2000. The virus is not shown to occur in Ireland with only a single case seen in the UK.

The literature review faced limitations. The most significant being a lack of current research into the circulation of variants of CPV. It would be suggested that Italy has an overrepresentation of CPV-2c as there is a significant amount of research on the topic by researchers such as N. Decaro, C. Buonavoglia & C. Desario. It can be said that certain countries had a limited amount of literature such as Ireland. The literature only looked into CPV and its variants in the south of Ireland in counties Cork & Kerry. This may be underrepresenting the prevalence of the virus in Ireland and also the circulation of CPV-2c in the country. Similar limitations can be seen in the countries of Czech Republic and Switzerland. These limitations should be taken into account when interpreting the data & highlight the need for further research to address these shortcomings.

Conclusion

In conclusion, this literature review has shown a broad range of knowledge concerning CPV-2 and its variants, CPV-2a, CPV-2b & CPV-2c. It has given an insight into the impact CPV-2 has had on control measures such as vaccination & research into the virus & variant prevalence & distribution within European countries. The findings have highlighted the importance CPV research in veterinary medicine & canine health. Understanding the distribution & clinical signs allows for better prevention strategies in practice. The review highlights the requirement of further research into the virus & its distribution with many countries having under representative samples. This will ensure the well-being of current & future dog populations within Europe.

Summary

Canine Parvovirus is a virus affecting dogs and has a morbidity rate of 100% & a mortality rate of 90% if left untreated. CPV-2's hallmark clinical signs include diarrhoea (+/- haemorrhagic), vomitus, lethargy & anorexia. Although these clinical signs are representative of the disease, it still remains vital to diagnose the disease via ELISA snap test or PCR to confirm diagnosis.

Although it was shown from the literature that CPV-2 has a higher occurrence in the German shepherd dog this must be understood to be an over representation as all dog breeds who are not or partially vaccinated are susceptible to infection.

From this review and data seen in literature used in the production of this thesis, males are the predominant gender affected by this virus, but this can also be viewed as an over representation, as any gender can be affected by the virus if not adequately vaccinated.

To prevent and manage outbreaks of CPV-2 it is vital to utilise vaccines on the market. The majority of vaccination used today are MLV vaccines which offer the best protection to canines. Vaccination protocols have been presented and recommended by manufacturers and the WSAVA.

This literature review mainly focuses on the distribution of CPV and its variants from 2007 to 2022 in various European countries, with the highest prevalence occurring in Greece, Italy, and the UK.

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Thesis progress report for veterinary students

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Name and title of the supervisor: Dr. Manczur Ferenc, Professor & Head of Department

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Thesis title: Literature Review: Epidemiological Assessment, Prevalence & Control Measures for Canine Parvoviruses in Europe

Consultation – 1st semester

	Timing			Topic / Remarks of the supervisor	Signature of the supervisor
	year	month	day		
1.	2022	09	20	Thesis topic plan	
2.	2022	10	28	Literature review planning	
3.	2022	11	24	Data collection plan	
4.					
5.					

Grade achieved at the end of the first semester: 5

Consultation – 2nd semester

	Timing			Topic / Remarks of the supervisor	Signature of the supervisor
	year	month	day		
1.	2023	03	03	Discussion of findings	
2.	2023	04	13	Discussion of literature review	
3.	2023	05	05	Discussion of results	
4.					
5.					

Grade achieved at the end of the second semester: 2

The thesis meets the requirements of the Study and Examination Rules of the University and the Guide to Thesis Writing.

I accept the thesis and found suitable to defence,

.....
signature of the supervisor

Signature of the student: .....

Signature of the secretary of the department: .....

Date of handing the thesis in 2023 November 6th

I hereby confirm that I am familiar with the content of the thesis entitled

Epidemiological Aspects, Prevalence and Control Measures for Canine Parvovirus in Europe

written by Ciarán Doherty

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Date: Budapest, 17 day 11 month 23 year

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