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Control of canine leptospirosis in Europe: time for a change?

W. A. Ellis

Changes in the formulation of the *Leptospira* components of dog vaccines are being considered in Europe, following changes in North America. This article discusses the options for change and recommends the continued inclusion of serovars *Icterohaemorrhagiae* and *Canicola* plus the inclusion of serovars *Bratislava* and *Grippotyphosa* (for mainland Europe only). If other serovars, such as *Pomona*, are to be considered in the future, then there is a need for additional clinical, cultural and serological studies across Europe to support their inclusion.

VACCINES for the protection of dogs against *Leptospira interrogans* infection have been available in Europe for approximately 50 years (Jull and Heath 1961). Traditionally, these have consisted of killed bacterins with two components – serovars *Icterohaemorrhagiae* and *Canicola*. Reports from mainland Europe indicate an altered epidemiological situation, and there have been calls for an expansion of the number of *Leptospira* serovars included in vaccines, to reflect the most prevalent serovars found in dogs (Gerlach and Stephan 2007, Geisen and others 2008). An increase in cases of leptospirosis in human beings in Germany has, in part, been attributed to a resurgence in canine leptospirosis (Jansen and others 2005) and has added to the calls for a review of vaccines. Changes in the epidemiology of canine leptospirosis in North America have led to the inclusion of serovars *Grippotyphosa* and *Pomona* in bacterins available there. In Europe, vaccine manufacturers are actively reviewing the strains of *Leptospira* that should be included in dog vaccines (Davies 2008) and, because major manufacturers have global interests, whether there is common ground between European and North American requirements.

Recent review articles have concentrated on the clinical signs, diagnosis and control of leptospirosis (van de Maele and others 2008, Jull and Heath 2008) and has added to the calls for a review of vaccines. Changes in the epidemiology of canine leptospirosis in North America have led to the inclusion of serovars *Grippotyphosa* and *Pomona* in bacterins available there. In Europe, vaccine manufacturers are actively reviewing the strains of *Leptospira* that should be included in dog vaccines (Davies 2008) and, because major manufacturers have global interests, whether there is common ground between European and North American requirements.

Epidemiology

Most of the information relating to leptospires in dogs is based on seroprevalence studies performed using the microscopic agglutination test (MAT). Although the serogroup is no longer a valid taxonomic term, it is used in this paper as it groups strongly antigenically related strains, allowing comparisons to be made between different studies that have been conducted using related but different serovars as antigens in the MAT. In addition, there is likely to be cross-protection between closely related strains.

The epidemiological picture varies across Europe, and direct comparisons between different studies are further complicated by the variability in minimum MAT titres used in different studies, ranging from 1:10 to 1:300. Although high titres (1:400 or 1:800) are useful for identifying the serovar strains that are likely to have caused recent clinical infections and for eliminating cross-reactions, they have limited value in assessing the levels of exposure within dog populations. In contrast, very low titres to serovars *Icterohaemorrhagiae* or *Canicola* could be a result of vaccination, and low titres to other strains could result from cross-reactions in the MAT.

In general terms, exposure to *Leptospira* appears to be low in vaccinated dogs in urban areas but much higher in rural dogs, dogs kept in large kennels or dogs from unvaccinated inner-city populations (Scanzi and others 2002, Modric and others 2008).

The major serogroups to which dogs in Europe are exposed are *Icterohaemorrhagiae*, *Grippotyphosa*, *Australia*, *Sejroe* and *Canicola*. The relative importance of *Grippotyphosa* and *Sejroe* group infections differs according to region within Europe, because these infections result from incidental exposure to strains maintained by rodent hosts whose distribution and concentration varies across Europe. *Icterohaemorrhagiae* infection is less subject to regional variation because its maintenance host – the rat – has a ubiquitous distribution. Serovars belonging to the *Australia* serogroup are maintained by wildlife hosts as well as by dogs, hence, exposure to these strains is consistently observed across Europe. *Canicola* infection is maintained in dogs, and is declining in many areas. Infection by other serovars, including those belonging to the *Pomona* serogroup (which is important in North America), are rare in Europe.

Serovars

*Icterohaemorrhagiae*

Where recent data are available, serogroup *Icterohaemorrhagiae* (serovars *Icterohaemorrhagiae* and *Copenhageni*) infection remains one of the most prevalent *Leptospira* infections to which dogs are exposed across Europe – in Germany (Geier-Dömling and others 2003, Geisen and others 2008), Croatia (Modric and others 2008), Denmark (Thøsen 2000), France (Andre-Fontaine 2000), Romania (Cârăan and Podor 2006), Greece (Burriel and others 2003) and Italy (Cerri and others 2003).

It is also the most common recognised cause of clinical leptospirosis in dogs, and in the UK cases are seen regularly by diagnostic laboratories, particularly in farm and sporting dogs. Given the ubiquitous nature of its maintenance host and the severity of clinical disease, there is an overwhelming case for the continued use of *Icterohaemorrhagiae* in dog vaccines.

*Canicola*

Serovar *Canicola* is maintained by dogs and has no other known maintenance host. The consensus view is that seroprevalence to *Canicola*...
is decreasing in many European countries (Claus and others 2008). This has been attributed to the use of vaccines for half a century. However, serological evidence of exposure in dogs still exists across Europe, and high seroprevalences have been found in some countries – 18 per cent in Romania (Cătană and Fodor 2006) and 21 per cent in Poland (Sobiech and others 1999). Clinical cases are still seen (Giejer-Dömeling and others 2003).

In the UK, clinical Canicola infection in dogs was common in the 1950s and 1960s but is now very rare. The last survey of unvaccinated dogs in the UK found that infection was still active in such dog populations, with a serological prevalence of 13.4 per cent and a cultural prevalence of 3.6 per cent (Van den Broek and others 1991).

The strains of Canicola found in the UK appear to have mutated in the late 1960s and/or early 1970s (Fig 1). Whether this was due to vaccine pressure or some other evolutionary pressure is unknown, but this change in the organism coincided with the virtual disappearance of clinical disease in dogs.

The risk of stopping vaccination against a host-adapted leptospirosis in its target host is that its prevalence may increase rapidly once population immunity falls; therefore, vaccination of dogs against serovar Canicola should continue.

**Grippotyphosa**

Serovar Grippotyphosa is maintained by a number of small rodent species in mainland Europe: the common vole (Microtus arvalis) (Fennestad and Borg-Petersen 1972, Boric and others 1982, Kuiken and others 1991), the root vole (Microtus oeconomus) (Chekhovic and others 1988), the muskrat (Ondatra zibethicus) (Desmecht and Smeets 1983), the grey vole (Microtus agrestis) (Modric and others 1991), and the common hamster (Cricetus cricetus) (Mochmann 1957). Serological data from the Czech Republic (Sebek and others 1983) and Slovakia (Tieml and Nesnalová 1993) suggest that the wood mouse (Apodemus sylvaticus) and the yellow-necked mouse (Apodemus flavicollis) may also maintain Grippotyphosa in some regions. The occurrence of Grippotyphosa in dogs is largely dictated by the occurrence of these hosts.

Seroprevalence studies have indicated frequent exposure to Grippotyphosa infection in a number of European countries, in particular, Germany (Gerlach and Stephan 2007, Geisen and others 2008), the Czech Republic (Balogh and others 1992), Slovakia (Tieml and others 1999), Poland (Sobiech and others 1999), Cmnia (Modric and others 2002), Switzerland (Rey 1987 and Italy (Scanziani and others 2002). As in North America, higher seroprevalences are seen in dogs from rural environments (Tieml and others 1989), reflecting the greater opportunity for direct or indirect contact with maintenance host species.

Grippotyphosa is one of the most common causes of clinical leptospirosis in dogs in Germany (Geisen and others 2007, 2008). There is clear evidence to support the inclusion of serovar Grippotyphosa in a dog vaccine for mainland Europe.

There is only tentative evidence of serovar Grippotyphosa in the UK. Twigg and others (1975) reported antibodies to serovar Grippotyphosa in 14 of 3959 wild mammals in Britain. These were mainly in A. sylvaticus (eight of 434 tested). They also found anti-Grippotyphosa antibodies in the sera of seven of 21 wild goats from Galloway. Antibodies to serovar Grippotyphosa have not been reported in the UK since. The situation is further complicated by the fact that a quality assurance ring test carried out in 1972 found that two of four UK contributing laboratories had mixed up their Grippotyphosa antigen with other serovars (W. A. Ellis, S. W. Machna, L. H. Turner, unpublished data). On the basis of this evidence, it would be very difficult to recommend the inclusion of a serovar not isolated in the UK in vaccines to be administered to dogs that remain in the country. However, the popularity of the Pet Travel Scheme means that increasing numbers of dogs are being taken to Europe with their owners, and there is an obvious case for these dogs to be given access to a vaccine with a serovar Grippotyphosa component.

**Bratislava**

Four closely related serovars (both genetically and in terms of their outer envelope lipopolysaccharide antigens) belonging to the Australis serogroup are found in Europe, namely serovars Bratislava, Lora, Jalna and Muenchen. Serovar Bratislava has been most commonly used as the antigen to represent the Australis serogroup in the MAT because it is the serovar most commonly isolated from domestic animals, and the strain isolated from dogs. Although the other serovars may also occur in dogs, they should not complicate considerations regarding the control of these serovars because, given their very close antigenic and genetic relationship, there would almost certainly be good cross-protection. As a consequence, the subsequent discussion refers only to serovar Bratislava.

Seroprevalence data from the past 20 years indicate widespread exposure of dogs to serovar Bratislava infection, both in Europe (Rey 1987, Brem and others 1990, Van den Broek and others 1991, Scanziani and others 2002, Cerri and others 2003, Gerlach and others 2007, Geisen and others 2008) and in North America (Stokes and others 2007). There are a number of known maintenance hosts for this serovar: hedgehogs, pigs and horses (Ellis and others 1983b, 1986). It also appears probable that dogs act as a maintenance host, given the widespread seroprevalence in populations that do not have access to the other recognised hosts, the low antibody levels in carrier animals (Van den Broek and others 1991) and the ability of the organism to persist in the kidney of carrier dogs for at least three months and in the genital tract of bitches (W. A. Ellis, unpublished data).

Acute clinical disease has been reported in Italy, and Mastorrilli and others (2007) reported a series of 16 acute clinical cases of serogroup Australis infection in which seven of the dogs either died or had to be euthanised. Adamus and others (1997) described chronic hepatitis in a single colony with serogroup Australis infection. Further strains belonging to the Australis serogroup were recovered from clinically affected dogs examined at the University of Zurich veterinary school (L. Corboz, personal communication); these have been examined at the World Organisation for Animal Health (OIE) Leptospira Reference Laboratory in Belfast and are very similar to 25 strains that have been isolated from UK dogs with either reproductive problems or nephritis (W. A. Ellis, unpublished data). Clinical disease is most likely to be apparent when large numbers of dogs are kept together, in breeding kennels, experimental facilities or long-term kennels. Given the emerging clinical picture and the widespread evidence of exposure to infection, there is a strong case for serovar Bratislava to be introduced into European vaccines.

**Pomona**

Two Pomona serogroup infections are found in Europe. The first, due to serovar Mozdok, is found across Europe and is maintained by a variety of small rodent hosts. From Denmark (Borg-Petersen and Fennestad 1956) through Germany (Ziers 1991) to Russia (Chernulka and others 1983) the maintenance host is the striped field mouse (Apodemus agrarius). Its host(s) in the westernmost parts of Europe are less well understood, but in Portugal, where an extensive study was carried out, the major hosts were the greater white-toothed shrew (Crocidura russula) and the Algerian mouse (Mus swards) (Collares-Pereira and others 2000). Serovar Mozdok has occasionally been isolated from cattle and pigs but has not been reported from dogs.
The epidemiology of serovar Pomona is less well understood. In the past, it has been isolated from domestic food-producing animals in Switzerland, Italy, Hungary and Bulgaria, and there are at least two reports of its isolation from dogs, in Hungary (Kemenes and Papp 1987) and Croatia (Modric and others 1987). Consequently, these isolations of serovar Pomona do not indicate evidence of infection in the major domestic species (pigs and cattle) or with animals that had been exposed outside the UK. There is no evidence of serovar Pomona infection in dogs, although sero-prevalences to the Sejroe serogroup (serovars Sejroe, Saxkoebing) or cattle (Hardjo). Two serovars, Saxkoebing and Hardjo, have been recovered from horses (Ellis and O’Brien 1988), a marker species in south-west England. This could be a reflection of the absence of small rodents in south-west England: from a field vole (Microtus agrestis) (Little and Salt 1975), common shrews (Sorex araneus) and a water shrew (Neomys fodiens) (Pritchard and others 1987b; Barlow 2004). Serovar Mozdok infection has been recognised in pigs (Pritchard and others 1997a, Barlow 2004) and as a possible cause of abortions in cattle (Flathawry and others 1984). Although these rodents are found throughout Great Britain, Mozdok infection has been confirmed only in south-west England. This could be a reflection of the absence of suitable studies in the rest of Great Britain. Twigg and others (1969) carried out extensive wildlife studies around Great Britain, but unfortunately none of their isolates was typed. The carrier hosts of serovar Mozdok do not occur in Northern Ireland. The absence of any known evidence of exposure of UK dogs to Mozdok may be a reflection of the lack of any appropriate studies in high-risk populations such as hunting dogs, farm dogs, particularly those with known infection.

The other Pomona serogroup strain found in the UK is serovar Pomona, which has been found only in Northern Ireland. Serovar Pomona has been recovered from horses (Ellis and O’Brien 1983), a sheep (Ellis and others 1983a) and from a monkey (W.A. Ellis, unpublished data). In all cases, there was circumstantial evidence to indicate that these probably resulted from exposure outside the UK or contact with animals that had been exposed outside the UK. There is no evidence of infection in the major domestic species (pigs and cattle) or in foxes and badgers, for which rodent species form part of the food chain. Consequently, these isolations of serovar Pomona do not indicate a possible risk to the local dog population.

Others Seroprevalences to the Sejroe serogroup (serovars Sejroe, Saxkoebing and Hardjo) have been reported in some countries. Seroreversion is a result of exposure to strains maintained by small rodents (Sejroe and Saxkoebing) or cattle (Hardjo). Two serovars, Saxkoebing and Hardjo, have been recovered from dogs in the UK. There is insufficient evidence of widespread infection or clinical disease in Europe to merit consideration of these serovars for inclusion in a dog vaccine.

Conclusions A major drawback to this review has been a lack of suitable clinical, cultural and seroprevalence surveillance data for at-risk dog populations in the UK, France, the Netherlands and the Scandinavian countries, and there is a need for this to be addressed using appropriate methods. However, it is safe to conclude that serovars Icterohaemorrhagiae and Canicola should continue to be included in dog vaccines in Europe. In addition, there is a good case for the inclusion of serovar Bratislava in vaccines, and, in the case of mainland Europe (but not in the UK), for serovar Grippoputkysphosa might be produced as a monovalent vaccine, which could be used as deemed appropriate by the licensing authorities. With regard to the Pomona serogroup strains, there is not a case equivalent to that in the USA for their inclusion in European vaccines.

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