# Dogs, Zoonoses and Public Health 2nd Edition

Edited by Calum N.L. Macpherson, François-Xavier Meslin and Alexander I. Wandeler



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2nd Edition



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# **2nd Edition**

Edited by

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# **Preface to 2nd Edition**

Since the first edition of this text was published in 2000, a number of important advances have been made in the fields of genetics, molecular biology and epidemiology, speciation, and immunology that have provided new insights into our understanding of the zoonotic infections humans share with dogs. The scope of the book has been expanded to include three new chapters, and all previous chapters have been updated and in some instances rewritten.

This 2nd edition provides an even more comprehensive account of the changing world and our culturally and individually diverse relationships with 'man's best friend', the domestic dog. The size of the world dog population is unknown but is positively correlated to that of the human population. Based on a number of observations it could be as high as one-tenth of the world human population, with 700 million dogs. A majority of those dogs, particularly in parts of Africa, Asia, the Middle East, and Latin America, are or are regarded as strays.

People's attitudes regarding dogs vary greatly from being only beneficial to humans to being a serious public health nuisance. As dogs are present and closely associated with humans and/or their activities in almost all places, most people will have a strong stand regarding their role and impact on human society.

A number of studies have demonstrated that the human–dog bond has a positive impact on human health, child development, and the quality of life. The use of dogs as companion animals, and companion animal medicine, are increasingly being recognized as important areas contributing to the betterment of human health. Dogs may permit people to live healthier, happier lives, and recent studies have shown the benefits dogs impart to many segments of the population including children, elderly people, those isolated by stigmatizing diseases such as AIDS, and the handicapped. Diverse groups of people in different parts of the world use dogs for sport and for hunting. They are valued for their ability to find prey in rainforests; great grassland areas; and in the frozen lands of the Arctic and Antarctic. In the latter dogs are also used for transport. In the extensive sheep-rearing areas of the world, such as in North and South America, northern and southern Africa, Australia, New Zealand, north-west China, Mongolia, and in much of Europe, dogs play an essential role in herding. Dogs are used in law enforcement: detecting people being smuggled across international borders, for sniffing out drugs and other illegal substances, and for crowd and individual control. Dogs have numerous roles in the medical field and are increasingly used as 'eyes' for blind people and 'ears' for deaf people. However, there are problems and dogs contribute to zoonotic infections and they foul pavements and public parks. They pose a public health nuisance through bites; harassment of pets,

livestock and wildlife; their persistent barking, particularly at night; scavenging from garbage sites; and their involvement in traffic accidents. The positive and negative attributes polarize people's opinions about dogs. Because of the strong opinions held on both sides it is difficult to get a balanced view, but whatever one's opinion, dogs are now an important part of our society in every corner of the world. Appropriate solutions to the issues, adhering with international animal welfare principles, need to be found: a number of solutions are provided in different chapters in this book.

The objectives of the 2nd edition of this book were to review the anthropological aspects of the human–dog relationship and to identify the benefits which may be derived from and attitudes vis- à-vis this association in different parts of the world, where cultural attitudes towards dogs differ greatly. This section is followed by a review of the current knowledge on dog population biology and ecology, also in the context of human populations, settlements, and activities. Attention is paid to the basis of the human–dog dependency; components within a dog population; and providing methods for calculating data, such as population size and turnover, essential for designing disease prevention and control programmes. A new chapter examines the nondisease-related issues posed by dogs, and this is followed by updated reviews on all the major viral, bacterial, protozoan, and helminth parasitic zoonoses shared by humans and dogs. The final chapters deal with dog and selected disease control and prevention aspects, including current and future methods for effective and humane dog population management.

The aim of the 2nd edition of this book is to provide, for those interested in dogs and the world we share with them, a comprehensive updated account of the complex public health aspects of this encounter. It also aims to examine how our interaction with dogs in different cultures and socio-economic conditions facilitates both beneficial and harmful processes, and how the zoonotic diseases are currently being controlled.

Calum N.L. Macpherson François-Xavier Meslin Alexander I. Wandeler

February 2012

# 1 The Human-Dog Relationship: A Tale of Two Species

#### Alan M. Beck\*

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Animals have generally played a great role in human ecological adjustment. Just as credible a reason as any for the domestication of animals is their use as pets. In other words, there is as much reason to believe that man's psychological needs were the primary cause for domestication of animals as that man needed to use animals for such material purposes as the saving of human labor and the satisfaction of a hunger for food. Boris M. Levinson (1969)

Many animal species usually share the same environment and often even benefit from each other's presence. They may follow one another for food or water, or flee together even when only one senses the danger. In natural symbiotic relationships, one participant does not significantly alter the physiology or behaviour of the other. This is not the case with people and their domesticated animals, and especially the human relationship with companion animals, people's pets.

### Domestication

Domestication was most probably promoted when humans were less mobile (from being nomadic), and new diet choices, cooking food, and the use of clothing was universal, setting the stage for plant and animal domestication (Leach, 2003).

Animal domestication is a biological process: the artificial selection (by people, not nature) of an animal's characteristics by breeding with the desired traits and discouraging, or prohibiting, the propagation of those animals without them (Darwin, 1859). This selective breeding alters the frequency of certain genes in the breeding population. The genes themselves are not altered (mutated), only their frequency of occurrence. The desired attributes will now occur more often, in time altering the characteristics of the whole animal population.

Physiological processes, and broad patterns of behaviour, are much less changed by selective breeding than are morphological characteristics. Hence, the gestation period, size of the genital organs, and social behavioural patterns of modern domesticated animals are basically the same as those of their wild ancestors, despite their differing appearance.

Many of the economic, social, and even aesthetic characteristics sought by people for their domesticated animals are more commonly observed in the younger individuals of the wild type. Perhaps without planning, people bred food animals such as pigs and cows that retained their more

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juvenile form. In growing, these animals did not expend energy on bone elongation, which meant a more efficient deposition of meat and fat on shorter bodies, which was of course what was desired. Initially, most domesticated animals were smaller than their wild ancestors, but later the domesticated forms were further manipulated to produce animals that were much smaller or even larger. Examples include Shetland ponies and Shire horses, which are smaller and larger, respectively, than their progenitors; the toy breeds of dogs, such as the Chihuahua; and the Newfoundland or Saint Bernard, which are actually larger than any wild canid. Sexually mature domesticated animals often have other attributes associated with the retention of juvenile characteristics, known as neoteny or pedomorphosis (Campbell, 1966). Neoteny is either early sexual maturation or retarded development of adult features, thus developing an animal that is sexually mature while retaining immature morphology (e.g. thinner hair, shorter horns, and smaller teeth) (Coppinger and Schneider, 1995; Darwin, 1859; Price, 1984, 1998).

Interestingly, neoteny is one of the ways living forms can evolve relatively quickly, for many inherited characteristics can be selected at the same time and the species can change more rapidly. It has been noted that human beings, Homo sapiens, have more in common with juvenile great apes such as gorillas and chimpanzees, than with full grown apes. The ability to stand erect, relative hairlessness, lack of heavy brow, and relatively short arms are characteristics of very young apes and adult humans. As the ape matures, the pelvis rotates and forces the animal to stand and walk using its arms as well as its legs; the animal becomes hairier; a heavy brow ridge develops; and the face, arms, and body grow to the proportions recognized as the adult form. Human beings, however, never outgrow their infantile characteristics even as they age and grow in overall size (Campbell, 1966, 1972; De Beer, 1958; Montagu, 1962).

In addition to infantile physical characteristics, humans possess many juvenile behavioural characteristics including staying with parents longer than the total longevity of most animals, and a need for touch and bonding more similar to that which most mammals exhibit only during their immature stage of development. The need to be part of a family even extends to a family-oriented social structure that may persist for the individual's whole life. The fact that the great apes outgrow these juvenile behaviours and physical characteristics is in part why none have been particularly successful as pets, despite their genetic relationship to us. Apes and all the larger monkeys are trainable and can be conditioned to tolerate the human way of life, but none thrive in it. Apes and the larger monkeys cannot remain house pets once they mature. In contrast, domestic animals, especially dogs, tolerate the human environment and even thrive with people.

Promoting the breeding of carnivores that retain their juvenile attributes encourages playfulness and less aggressiveness, making them better companions and easier to handle. In addition, such a breeding programme would also promote other juvenile traits usually considered more attractive. Most people find animals with wide eyes and short snouts pleasing (Glocker *et al.*, 2009; Lawrence, 1989; Lorenz, 1943). These are typically features of the young. Many of the animals that are particularly enjoyed by our culture are those that retain some of the physical attributes of the young, such as the seal, dolphin, squirrel, and cartoon characters (Gould, 1979).

Animals were domesticated, for one reason or another, because we liked them. Therefore, many of today's domestic animals were created by selectively breeding animals that retained the traits of the young, for example, cattle, pigs, dogs, and to a somewhat lesser extent, cats. All of these retain many body characteristics and behaviours of the juvenile throughout their lives.

It was assumed that early humans selected their animals for tameness, a trait appreciated by all who must manage an animal. Dmitry K. Belyaev (1917–1985), like Darwin (1859), noted that all domesticated animals exhibit the same variations in size (can be smaller or larger than an ancestor); hair (piebald, lacking pigmentation in some areas); tails (curly); ears (droopy); and can mate more than once a year (Belyaev, 1969; Trut, 1999). Darwin (1859) noted that, 'Not a single domestic animal can be named which has not in some country drooping ears; and the view suggested by some authors, that the drooping is due to the disuse of the muscles of the ear, from the animals not being much alarmed by danger, seems probable.' (Darwin did not appreciate that droopy ears is the retention of a juvenile trait.) In 1959, Belyaev (1979) began an experiment that proved domestication. Once a month Belyaev observed bred wild-caught silver foxes (Vulpes vulpes) during their first 6 months, selecting those that made nonaggressive contact with other pups or humans. At 7–8 months of age (maturity) he scored for tameness, friendliness, wagging of tails or whining to attract attention. Only about 10% of wild foxes display a lack of fear or aggression in captivity. By 10 generations 18% of the selected foxes were extremely tame, and by 20 generations 35% foxes were extremely tame. The tamed foxes had floppy ears with shorter tails and legs and piebald coats. Apparently domestication (with the juvenile characteristics and behaviours) of a wild canid can occur within 20 animal generations, just by selecting for accepting human captivity and social contact (Belyaev, 1969, 1979; Trut, 1999). The domesticated foxes also possessed some of the social cognitive skills observed in today's domestic dog (Hare et al., 2005).

Early humans, whose strategy for survival included much collaboration, were selected for tameness thus also selecting for a naturally occurring neoteny; this allowed humans to evolve rapidly away from their primate ancestors, avoiding the competition which we humans may not have won. Humans, with their juvenile qualities, maintain behaviours more typical of the young. Hence, they extend parenthood and closeness with each other and pets; in other words, human social order and culture. Man, not dog, is man's first domesticated animal.

#### The Ancestor of the Dog

It is now generally accepted that dogs, *Canis familiaris*, were first tamed then domesticated from the wolf; probably one of the smaller

subspecies of *C. lupus pallipes*, or the nowextinct *C. lupus variabilis* (Clutton-Brock, 1995). Wolf domestication started in the late Mesolithic (15,000 years ago) after humans built houses, farms, and settlements (Driscoll *et al.*, 2009). It is generally accepted that a true relationship between humans and dogs began in prehistoric times, some 12,000 years ago, though some feel it may have been even earlier (Shipman, 2009). Sheep and goats are traced back approximately 10,000 years, cats about 5000 (Morey, 1994).

As prehistoric peoples travelled from place to place in search of game and fertile lands, wild wolves undoubtedly followed, attracted by the prospect of an easy meal on the bones, uneaten food, and even the human waste people left behind. At this stage the wolf was not so much loved as tolerated. An uneasy symbiosis must have developed. Wolves warned humans of approaching danger and may have even led early hunters to animals that both could eat. Taming occurred as individual animals were rewarded with food when they approached. Tamed animals could be captured and bred. Keeping the offspring of those animals particularly being tame led to animals with the juvenile qualities people wanted – the domestication process.

The innate response for dogs to accept people was bred, but dogs still retained much of the behaviours of the pack-oriented animal. In time, dogs responded to humans as members of their pack and treated them more as their conspecifics (members of the same species). The conventional definition of a pack implies members of the same species, as the conventional definition of aggression implies a conspecific interaction. If we extend both these concepts to include ecological and social 'conspecifics', if not necessarily genetic conspecifics, we can explain a great deal of our interactions with domesticated dogs. Dogs appear to be evolving to be even better adapted to their human-dominated environment. Dogs, alone among animals, can now recognize where a human is pointing (Hare, 2007; Hare and Tomasello, 2005; Hare et al., 2002); recall their owner's face when hearing the owner's voice (Adachi et al., 2007); and imitate an owner's behaviours (Range

*et al.*, 2010); however, dogs do not necessarily seek help in an emergency (Macpherson and Roberts, 2006).

The first extension of the dog-human pack hypothesis would be that a dog and its owner (master) are a true social group. From the human's point of view, the dog is a 'member' of the family; indeed, most people who are dog owners specifically refer to their animals as a member of the family (Beck and Katcher, 1996). Most people intuitively respond to a dog's 'play-soliciting bow' or growl in much the same way another dog would. It is this preference to exist in a pack, dominated by a leader, that forms the basis for many successful human-dog relationships. When there is a lack of a clear hierarchy or when the animal, not human, is the leader, we see problems in the family, including animal bite and inappropriate behaviours.

The rate and range of changes that distinguish the dog from wolf or even from one dog breed to another has been increased by selective breeding within relatively small populations. Dogs were bred to meet the demands of differing climates and roles (Coppinger and Coppinger, 1996, 1998). There is no one reason for the domestication or even keeping of dogs. Nevertheless, dog keeping is common around the world.

#### The Dog Population

The dog population in urban and suburban areas is composed of three interacting, and at times interchangeable, subpopulations:

**1.** pets that never roam without human supervision;

**2.** straying pets that roam continuously or sporadically; and

**3.** ownerless animals usually referred to as strays.

The progeny of true strays are feral dogs. Social attitude towards strays and feral dogs is ambivalent. On one hand, they are protected because society is unwilling to either socially or financially support animal control and, on the other hand, they are unfairly blamed by popular literature as the major cause of dog bite injuries and attacks on livestock (Beck, 1980).

Estimates of the total dog population come from local, regional, or national surveys and there is considerable variation in methods used. Most relied on surveys of consumer panels and estimate about 78.2 million owned dogs. Today, more than 62% of US households have companion animals and 42% have more than one animal (American Pet Products Manufacturers Association, 2011). In Australia, approximately 60% of the 6.2 million households have one or more pets; 53% of the households have either a dog or a cat (Heady, 1999; McHarg et al., 1995). Dog, cat, and/or bird ownership in European households; 71% in Belgium, 63% in France, 60% in The Netherlands, 55% in Britain, 61% in Italy, 37% in Germany, and 70% in Ireland, averaging 52% for all 17 European countries surveyed (Reader's Digest Association, Inc., 1991).

By contrast, there are relatively few studies of urban stray or feral dogs. Specific populations have been studied in Baltimore, Maryland (Beck, 1975, 2002), St Louis, Missouri (Fox *et al.*, 1975), New York City (Rubin and Beck, 1982), Berkeley, California (Berman and Dunbar, 1983), Italy (Hansen, 1983), Newark, New Jersey (Daniels, 1983a, b), and some areas in Mexico and the American south-west (Daniels and Bekoff, 1989).

As a general rule, straying pets are more common in high human density, low-tomiddle-income areas, especially where people have direct access to the streets (e.g. areas of low-to-middle-income private housing or row houses). Ownerless strays are more common in low-density, low-income areas where there is shelter and fewer requests for animal control, such as around parks, dumps, or abandoned parts of the inner city (Beck, 2002; Fox *et al.*, 1975; Nesbitt, 1975; Scott and Causey, 1973).

It is important to distinguish straying pets from ownerless strays, because they cause different problems for society and are managed or controlled by different means (Beck, 1974). Straying pets are best managed by encouraging and enforcing responsible ownership, while strays are controlled by capture and alterations of the environment, such as the boarding-up of vacant buildings, and clearing dumps and urban lots (Beck, 1981).

One adaptation of unowned stray dogs in an urban environment is to behave like socialized pet dogs (Fielding *et al.*, 2005; Rubin and Beck, 1982). In that way they are indistinguishable from owned roaming dogs and are tolerated as loose pets and not wild dogs – a form of 'cultural camouflage'. Therefore the differences between owned and unowned stray dogs are not easily observed without extensive study

No country has an official census of their pet or feral dog population, although methods exists for those interested in animal control or public health (Beck, 1982; Bögel, 1990), and there are statistical models to assess the owned population (Patronek *et al.*, 1996, 1997; Patronek and Glickman, 1994; Frank, 2004). There are no precise figures of the number of animals killed in animal shelters. In the United States, estimates range between 2 and 6 million for dogs and cats killed in animal shelters each year (Rowan, 1992). The popular press still often quotes figures in excess of 12 million.

By domesticating the dog, people assumed responsibility for its survival, and in common with other domestic animals, the dog does not do well without the intervention of humans. In urban areas stray dogs do not reproduce well enough to establish a wild population, and so soon disappear if people do not abandon pets (Beck, 2002).

## Social Conflicts of Dog–Human Contact

Most of the problems associated with animals in populated areas concerns dogs. The major issues associated with dogs in cities include animal bite, environmental damage, potential disease, and humane considerations for the animals themselves. These are real issues but there are also real solutions.

#### Dog bites

One concern about dogs in cities is that they may bite people, especially children. All of the US studies using reported bite-rate data show the same pattern: people aged 4–19 receive about 20% of all dog bites (Beck, 1991; Beck *et al.*, 1975; Hanna and Selby, 1981; Harris *et al.*, 1974; Lauer *et al.*, 1982).

Contrary to public perception, in the United States the owned pet dog, not strays, leads the pack in bite rate. Dogs owned by the neighbour of the victim have the highest rate, followed by those owned by the family of the victim. Strays had the lowest rate. However, bites from strays are more commonly reported than bites from owned animals. Where there is good reporting of all bites, for example in population-based surveys or on military bases, non-owned or stray dogs account for less than 10% of all bites (Beck, 1991). One reason for the disproportionate 'over-reporting' of strays is the perception that strays cause more disease, such as rabies. Therefore, people tend to seek medical care and report the bite more frequently when bitten by an animal whose owner is not known; 50% of people bitten by dogs without known owners sought medical treatment, compared to only 29% of people bitten by family-owned dogs, and 39% when the dog was owned by a neighbour (Beck and Jones, 1985). In the United States, the fatal dog bite problem is increasing, mainly because of the increasing ownership of pit bull-like dogs, which account for nearly 60% of fatalities (Beck, 2007; Bini et al., 2011; Sacks et al., 2000). All fatalities have been from owned dogs.

Considering the patterns of dog-bite injury, it is not surprising that a leash law, in one form or another, is common in many cities around the world. This simple regulation is a way of reducing animal bite and many of the problems associated with dogs. The law should set a maximum length of leash – about 1.8 m (6 feet) or less. People should not tether their dogs on ropes too much longer than this; longer leads can endanger the animals, which may become entangled.

Dog bite can be serious, as many infectious agents have been identified at the site of a bite (Talan *et al.*, 1999), and death from trauma has been reported (Bini et al., 2011; Borchelt et al., 1983; Pinckney and Kennedy, 1982; Sacks et al., 2000). Nevertheless, serious infection and fatal injury are rare. With the exception of the potential of rabies, the vast majority of bites are no more serious than the slips and falls associated with childhood indeed, the injuries associated with routine child play are more common (Weiss et al., 1998). But we should always try to minimize bite injury. The safest and most humane way to reduce bites from dogs is a public health policy that encourages having dogs that are well socialized to people, and keeping dogs on a leash or always having them supervised when on public property.

In the United States, stray dogs continue to have little impact on human public heath, be it from animal bites (Beck, 1991) or rabies (Beck *et al.*, 1987; Torrence *et al.*, 1995). For some people, ownerless dogs are part of the urban scene that live out their lives as wild canids. For others, strays are animals that must be captured as pests and removed from life on the streets, after which they are usually killed, although some are adopted and become owned pets.

Owned dogs with undesirable behaviours, such as biting, are more likely to be relinquished to an animal shelter. Compared with dogs having no unwanted behaviour, those exhibiting undesirable behaviours daily, such as barking, chewing, hyperactivity, inappropriate elimination, aggressiveness toward other pets, and aggressiveness toward people, have a higher risk of being relinquished to an animal shelter, Odds ratio = 1.3 versus 8.5 (Patronek et al., 1996). Controlling the conflicts between the owner's expectations and the dog's nature is one of the important issues in public health and animal welfare. Avoiding owner-dog conflicts is one of the most efficient ways to lessen relinquishment of dogs to animal shelters and reduce dog bites.

aesthetic problem. Dog faeces in public areas allow parasite transmission from dog to dog, and are also a human public health issue.

There are numerous studies establishing that dogs are frequently parasitized by *Toxocara canis*, and failure to clean up after dogs seeds the environment with *Toxocara* eggs. It is now widely recognized that the ingestion of embryonated *Toxocara* eggs can cause human illness such as toxocariasis or visceral larva migrans. The disease appears to have two forms, one involving an intestinal migration and the other having ocular involvement (Glickman and Shofer, 1987).

The best way to lessen the occurrence of parasite contamination is routine veterinary care. Animals that are routinely 'de-wormed' do not pass contaminated faeces, which is particularly important for those dog owners with young children. Dog waste, apart from being a source of parasites, is viewed as a kind of environmental pollution. To address this problem, most large metropolitan areas in North America and Europe have laws that restrict the activity of animals, especially dogs, in public areas. Most cities in the United States prohibit pets from entering restaurants or food stores, or going on public transportation, except for animals in enclosed carriers or service dogs assisting people with special needs.

One of the most common regulations to reduce dog waste in public areas is to encourage or require dog owners to have their dogs use the street, rather than sidewalk, for defecation, the so-called 'curb your dog' laws. In this way people do not step into waste, which is carried to storm drains during street washing or rain. In addition, most cosmopolitan centres encourage or enforce 'scoop laws' so owners clean up after their dogs in public (Beck, 1979; Brandow, 2008). Basic courtesy permits dogs and people to share the cities in ways that benefit both.

#### Dogs and disease

With the exception of rabies, most of the diseases transmitted from dogs to humans do not attract much public attention. However dog waste, a perennial nuisance in cities, is more than just an

## The Social and Health Benefits of Dogs in Society

Dogs are present in almost all human settings, and many share the human home as well. For some, they replace the children who have grown and moved away or perhaps were never born, and for others, they are playmates for the children still at home. In the United States, more than half of the families with a dog also have children at home. At the very least, for some people, dogs afford increased opportunities to meet other people. We are beginning to understand this complex bond between pets and people; two species with the common goal of surviving and enjoying life together (Beck, 1999; Beck and Katcher, 2003, 1996; Beck and Meyers, 1996).

People with good human contact are healthier than those who are isolated from others (Lynch, 1977, 2000). Because pet animals, especially dogs, are perceived as members of the family, pet ownership is one way people can be protected from the ravages of loneliness (Beck and Katcher, 2003, 1996; Katcher and Beck, 1986). Unlike talking to other humans, people experience a decrease of blood pressure when talking to pets, indicating that they are more relaxed with them than with people (Katcher et al., 1983; Baun et al., 1984; Wilson, 1991). Even in the presence of unfamiliar dogs, people experience a temporary decrease in blood pressure (Friedmann *et al.*, 1983).

In 1980, there was the first epidemiological report documenting the value of pet ownership. A study of people hospitalized after a heart attack found that 94% of those who happened to own pets were alive after the 1st year compared with 72% of those who did not own any animal. The ownership of any animal correlated with improved survival. A discriminate analysis demonstrated that pet ownership accounted for 2–3% of the variance (Friedmann *et al.*, 1980). While 2–3% may seem small, the impact, considering the frequency of heart disease, is significant and cost effective.

A more recent study of the benefits of interactions with animals found that pet owners had reductions in some common risk factors for cardiovascular disease when compared with non-owners (Anderson *et al.*, 1992). Pet owners had lower systolic blood pressures, plasma cholesterol, and triglyceride values. While pet owners engaged in more exercise, they also ate more meat and 'take-out' foods than non-owners, and the

socio-economic profiles of the two groups were very similar. It appears that pet ownership may reduce the risk factors associated with cardiovascular disease, possibly for reasons that go beyond simply an association with risk behaviours.

Serpell (1991) reported that dog owners experienced fewer minor health problems and increased the number and duration of their recreational walks. The effects persisted over the 10-month study period and there was no clear explanation for the results. Naturally occurring events in people's lives are enhanced because of animal companionship. For instance, people walking with their dogs experience more social contact and longer conversations than when walking alone (Johnson *et al.*, 2011; Messent, 1983).

In a study, nearly 1000 non-institutionalized older adult Medicare patients were evaluated prospectively. Those subjects who owned pets appeared to experience less distress and required fewer visits to their physicians than non-owners. While animal ownership generally had value, the most remarkable benefits to health were for those who owned dogs (Siegel, 1990). Most of the people noted that the pets provided them with companionship and a sense of security, and the opportunity for fun/play and relaxation. Animals allowed people to experience bonding. Siegel (1993) suggested that pets have a stress-reducing effect. The elderly often benefit the most from the companionship of animals (Dembicki and Anderson, 1996). Consequently, support has grown for protecting the right of pet ownership for older adults living in the community, and encouraging animal contact for those in long-term nursing home settings. There is continued growing evidence documenting the health benefits of animal interaction (Barker and Wolen, 2008).

# The use of animals in therapeutic settings

Long before there was any evidence that animal contact enhanced physical and mental health, animals were being used in therapeutic settings, referred to as 'animalfacilitated therapy' or AFT. Much of the early literature documents nothing more than fortuitous interactions with animals that happen to be present in a therapeutic setting (Beck, 1985; Beck and Katcher, 1996). The animals, mostly dogs, were originally included in the setting to provide the expected comfort traditionally associated with pet care. Often the best 'medicines' are appropriate concentrations of what is generally beneficial (Beck and Katcher, 1984). From the very beginning AFT has paralleled the use of animals as pets and many of the therapeutic uses are extensions of the health benefits now recognized for those who own or interact with companion animals. The most common kinds of AFT programmes are:

**1.** institutionally based programmes where animals either reside in the facility or are brought by visitors;

**2.** non-institutional programmes for older adults where animal contact is facilitated in people's homes;

**3.** service animals for the disabled in the home setting using specially trained animals, usually dogs; and

**4.** horseback riding (equine) programmes providing riding directed towards physical therapy.

The most common therapeutic animal is the dog. Today, AFT programmes occur throughout the developing world.

A survey of 150 selected US and 74 Canadian humane societies found that 49 (46%) of the US and 49 (66%) of the Canadian society programmes ran AFT programmes. More than 94% used dog and/or cats, 28% rabbits, 15% small mammals, and 10% birds (excluding poultry) in their programmes. More than 48% of US and 43% of Canadian programmes consulted health professionals about zoonotic prevention. Nearly 10% of community-based and 74% of hospitalbased programmes had printed guidelines. Potential problems involve rabies, *Salmonella* and *Campylobacter* infections, allergy, and ringworm (Walter-Toews, 1993).

While AFT has a good safety record, there are greater risks as programmes involve more people. Potential exists for zoonotic infectious or parasitic disease, bite injury, accident, or allergy. Prevention can be addressed by:

1. proper selection of animals;

**2.** not including people who are allergic to animals;

**3.** having comprehensive infection-control programmes in the setting;

**4.** having pet policies with advice from public health veterinarians; and

**5.** developing a surveillance and response programme (Schantz, 1990).

Future research will improve both the safety and efficacy of the use of animals in therapeutic settings.

#### Conclusion

Dogs have been part of human households ever since people began living in villages some 12–15,000 years ago. Interactions with dogs may very well be one of our more successful strategies for survival. Today, dogs continue to play a major role in the lives of people around the world. While the medical history of our relationship with animals, including dogs, mostly documents the detrimental effects of animal contact - including infectious diseases, zoonoses, parasitism, and injury from bites - there is long history of healthy interaction. While animal contact carries risks, the frequency of most zoonotic diseases can be lessened, perhaps even eliminated, with animal management practices that would serve both humans and the animals themselves. Veterinary care to manage bacterial, viral, and parasitic infections; mechanical restraints such as leashes and cages; selective breeding; responsible legislation; and owner education have made animal ownership a safe, healthy, and rewarding experience for many. Modern and sensitive public health policy would also help many enjoy dogs while protecting the public's health. There is substantial evidence to support the positive benefits of animal companionship for various segments of the population, especially children, the elderly, socially isolated, and the handicapped. More research needs to be directed to establish

both the scope of these benefits and ways to channel the information more effectively to improve the public health of the community. In addition, more research is needed on how to better incorporate dogs for those in urban centres, so both the animals and people can enjoy improved physical and psychological health.

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# 2 Benefits of the Human-Dog Relationship

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The dog (Canis familiaris L.) is without a doubt the oldest domesticated animal species and has accompanied man<sup>1</sup> some 15,000 years; the oldest faunal remains worldwide definitively determined to be from the domesticated dog were found in Kesslerloch Cave in Switzerland, and dated at c. 14,000–14,600 BP (Napierala and Uerpmann, 2010). Mithen (1998) has proposed that interactions with dogs in prehistoric hunter-gatherer societies have even shaped the way we think. Theories of domestication, that is, the reasons why man domesticated the wolf, are diverse, but there is now widespread agreement that the dog was not kept for economic reasons, but rather as a 'companion' animal (Messent and Serpell, 1981; Serpell, 1986, 1995; Beck, 2000). Nevertheless, Coppinger and Coppinger (2001) have stressed the importance of selection for working roles in the further development of the dog.

Most of the chapters in this volume deal with 'negative' aspects of dog-human relationships and humane ways to reduce or eliminate those problems. It is therefore important to summarize the positive aspects, the benefits of human-dog relationships, from the outset. Although no longer the most popular companion animal in many countries, pet dogs can be found in every country of the world irrespective of their level of economic development or religious heritage.

Three theories have been drawn upon to explain both the universality of the humanpet-(dog-) relationship as well as the therapeutic benefits animals provide many persons:

attachment theory (see Bowlby, 1969);
 social support theory (Collis and McNicolas, 1998; McNicolas and Collis, 2006); and
 'biophilia' or the 'biophilia hypothesis' (Wilson, 1984; Kellert and Wilson, 1993).

Attachment theory is chronologically the oldest potential explanation and is based upon the first social relationship between an infant and the mother. The presence of the mother (or a partner) is reassuring, while separation promotes anxiety, stress, and contact-seeking behaviour. Social support theory has been applied to the humananimal bond since the mid-1990s: in times of need we seek support (emotional or tangible) from our social support network to help cope. Companion animals can provide social/emotional support, either as members of the network or even replacing a human member in the network for some people. The biophilia hypothesis claims that humans are innately attracted to nature – plants, animals, and natural scenes.

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The innate releasing mechanism called the 'Kindchenschema' (infantile appearance of animals which elicits nurturing behaviour) and the universality of nurturing behaviour – taking care of and adopting young or sick animals – speak for this explanation.

## General Effects of Animals, Especially Dogs, on the General Public: The Benefits

In the last three decades research has provided solid evidence for the positive effects of dogs on the health and well-being of people of all ages.

Serpell (1991) found in a prospective study that the acquisition of a pet (dog or cat) significantly reduced complaints about minor health problems and improved measures of quality of life relative to a control group over the same 10-month period. The effects remained significant for the new dog owners over the entire period, but the improvements disappeared somewhere between 1 and 6 months for the new cat owners. He also found an increase in walking activity by the dog owners.

Friedmann and Thomas (1995) found that both high social support and pet ownership predicted one-year survival rates after hospitalization for acute myocardial infarction independently of physiological severity, demographic, and other psychosocial factors. Dog owners were significantly less likely to die within 1 year than non-owners.

Anderson et al. (1992) conducted a free screening clinic for cardiovascular disease risk factors (over 5000 participants) and found that pet owners had lower levels of accepted risk factors (blood pressure, plasma triglycerides, plasma cholesterol) than non-owners. This was not explicable on the basis of differences in smoking habits, diet, BMI, or socio-economic profile. Somewhat later Jennings et al. (1998), working from the same laboratory, found that dog owners visited a doctor over the previous year 8% less often than non-dog owners, while cat owners did so 12% less often than non-cat owners (both reductions significant). This was presumably related to lower costs for health care, which was later substantiated by Turner (2004) based on a government survey of over

9000 randomly selected Swiss households reporting all income and expenditures over a 1-year period.

Ascione and Weber (1996) and Beetz and Ascione (2004) have shown that increasing empathy towards companion animals (including dogs) increases empathy towards other people, and that the effects are longlasting. The latter study also found a correlation between empathy towards animals and emotional intelligence.

Dogs especially have been shown to function as social facilitators of increased contact with other persons, and the robustness of this effect has been demonstrated by McNicolas and Collis (2000). This has been demonstrated for children, adults (Hart, 1995a), and especially for the elderly (Hart, 1995b; Wilson and Netting, 1987), for physically challenged persons, and for non-communicative patients in psychotherapy.

A multitude of studies demonstrates that companion animals provide important emotional social support to children (Bryant, 1985; Covert et al., 1985; Melson and Schwarz, 1994; Rost and Hartmann, 1994). Bodsworth and Coleman (2001) found that children in single-parent families had significantly higher levels of attachment to their dogs than children in two-parent families, especially in the early childhood stage. In the urban, multicultural school classroom, studies in Vienna have shown that a dog resting quietly on its blanket in the corner results in fewer aggressive outbreaks, and improved social integration and an improved learning environment (Hergowich et al., 2002; Kotrschal and Ortbauer, 2003). For these reasons, the IAHAIO (2001) has unanimously passed its 'Rio Declaration on Pets in Schools', which was also endorsed bv the WHO-IAHAIO-WSPA Training Programme on Zoonoses and Human-Animal Interactions in Sao Paulo, Brazil, the same year (World Health Organization, 2001). Further, Spiegel (2000) showed that an elementary school-based dog bite prevention programme was quite effective.

Finally, concerning people in the general public, Allen *et al.* (1991) and Allen (1996) have found that a pet dog is more effective as a moderator of autonomic responses to stress in adults than human partners or friends.

## Therapeutic Effects of Animals, Especially Dogs: The Benefits

Animals, especially dogs, have been successfully involved in animal-assisted interventions to help people with various health problems. As this is not the main topic of this chapter, yet still related to the benefits of dogs to humans, only a brief summary with exemplary literature references are listed in Box 2.1.

Most recent reviews of the positive effects of companion animals, especially dogs, on human health and well-being were produced after an international conference organized by the US National Institute of Child Health and Human Development (NICHD) and the WALTHAM Centre–Mars Inc. in 2008 (McCardle *et al.*, 2011a, b).

## Public Attitudes to Dogs: An International Comparison

Turner (2010 and in preparation) has conducted a cross-cultural comparative study of adult attitudes towards animals in 12 countries,<sup>2</sup> from which results concerning dogs are presented here. Results comparing attitudes between French- and German-speaking Swiss adults have been published elsewhere (Fehlbaum *et al.*, 2010). Over 6000 questionnaires were distributed and recollected from adults in urban and suburban areas of major cities in these countries. Volunteers from many animal protection societies and shelters, human–animal bond organizations, veterinarian associations, university students, and colleagues collected the completed questionnaires.<sup>3</sup> Besides demographic information on the participant, the questionnaires contained 27 statements (five of which were control questions to assess understanding of the statements and seriousness of questionnaire completion) in the local language, with which the volunteer participants had to agree or disagree in a 5-point Likert scale. ANOVAs were conducted to assess the effects of four factors: location (country) and religious heritage; gender of the person; pet ownership (current or previous); and sample type (convenience: 'random' sample or 'animal friend' sample, e.g. from a vet practice or dog shelter waiting room). Only significant differences are reported.

On the statement 'Keeping animals as pets brings many benefits to the person' all four factors were significant (see Fig. 2.1). Non-pet owners, men and 'random' persons, although agreeing with this statement, were less in favour than pet owners, women, and the sample connected with animal-friendly institutions. Although people from all religious backgrounds agreed with the statement, Jews agreed more strongly than people of all other religions. Christians also agreed more strongly than those of all other religions except Muslims, who differed significantly from Christians but answered between Jews and Christians.

For the statement 'Dogs are very likeable animals', again all four factors were significant. Women, 'animal friends', and pet owners agreed more strongly with this statement; Muslims, while still agreeing, did so significantly less strongly than people of all other religions except Hindus, while Jews were the most dog-friendly group. Additionally, the statement 'Dogs make ideal pets' was more strongly agreed to by pet owners and people questioned in animal-related institutions,

Box 2.1. The health conditions for which animal-assisted interventions have been successfully applied.						
Aphasic patients in psychotherapy (Corson <i>et al.</i> , 1977)						
Persistent vegetative state, apallic syndrome (Röger-Lakenbrink, 2006)						
ADHD and Conduct Disorder children (Katcher and Wilkins, 2000)						
Down Syndrome (Limond <i>et al.</i> , 1997)						
Autism spectrum disorders (Grandin et al., 2010)						
Alzheimer patients (Bateson <i>et al.</i> , 1998)						
Neurological/motor dysfunction (Röger-Lakenbrink, 2006, pp. 129–132)						
Physically challenged persons (Allen and Blascovich, 1996)						



**Fig. 2.1.** Agreement with the statement 'Keeping animals as pets brings many benefits to the person' a) by religion and b) by sex and sample type.

Muslims significantly less strongly – but still in agreement.

Two final statements are of interest to organizations dealing with abandoned, suffering animals: 'If an animal is suffering (pain or incurable disease) and cannot be cured, it should be killed *painlessly*'. Only religion was a significant main effect here. People of all religions (including Buddhists) agreed, but Christians and Jews agreed significantly more strongly than the others. And finally, 'In this country (where I am now), stray dogs are no problem'. In London, England (n = 353), 46.6% agreed or strongly agreed, with 17.8% neither agreeing nor disagreeing. In India (here the survey was conducted in both Mumbai and Chennai, n = 827), 34.4% agreed or strongly agreed, with 13.3% being neutral. It would appear that stray dog control programmes have been relatively successful in London.

In cities of India fewer people agree than in London, but a higher proportion of the sample also disagrees, indicating a polarization of opinions. But we caution that there are probably enormous differences in how people define 'stray dogs' in cities of the two countries.

### Behaviour towards dogs on the street: A comparison between Amman (Jordan), London (England), and Chennai (India)

In the second phase of the cross-cultural study described above, direct observations with behavioural data were collected from random encounters between people and dogs in the urban areas of Amman, London, and Chennai (as well as between people and cats and other animals, but these are not discussed here) (Fig. 2.2). Economically comparable areas<sup>4</sup> of all three cities were selected and each day different routes were selected randomly, but at times of day when one might expect to see more encounters between animals and people on the streets. The routes were walked (occasionally in Chennai driven at 15km/h which was factored into the census data), and whenever an animal was spotted, observed from a distance of ca. 20 m as a 'focal animal' for random encounters with different pedestrians as long as it remained in view, usually about 10 min. Behaviour of the persons and animal were recorded on a concealed Dictaphone® using earphones (simulating talking on a cell phone or listening to music), and later the same day transcribed onto defined data sheets before being typed into Excel<sup>®</sup> files for later analysis. Due to differences in the number of observation days/minutes in the three cities, data were adjusted for the number of animals or observations per hour of observation time in the statistical analyses.

As shown in Table 2.1, 3.5 dogs/h of observation were noted in Amman (as opposed to 11.3 cats/h); 17.5 dogs/h were recorded in London; and 14.0 dogs/h were seen in Chennai. Of course, Amman, Jordan, being a Muslim culture, was expected to be more cat friendly and less dog friendly. However, the first author and observer were surprised to note how friendly and well-kept the cats on the suburban streets of Amman were. Further, the owned

dog population in Amman is increasing (M. Ledger, Humane Center for Animal Welfare, pers. comm.), notably since HRH Queen Rania was pictured in the local press stroking a dog at the opening ceremony of the new centre.

Even though the figures below also show data on dogs in Amman, the sample size for dogs there was too small to interpret; therefore, we now concentrate on a comparison between Chennai and London. An ANOVA of pedestrian eye contact with the dogs on the streets with post-hoc tests (Fig. 2.3) revealed a significant city effect and that Chennai differed significantly (much less eye contact).

Comparing the level of control over the dogs encountered, the situation is the opposite in Chennai and London: more free-roaming (street) dogs in Chennai, more leashed or controlled dogs in London. Of the street dogs encountered in Chennai, 60% had a notched ear, indicating that they had been captured, sterilized, immunized against rabies, and returned to the street. In London, about twice as many persons encountering a dog as in Chennai greeted it or the owner. In Chennai, the majority of dogs is not under human control and received less attention (eye contact) than leashed/controlled dogs. Leashed/controlled Chennai dogs still received less eye contact than leashed/controlled dogs in London.

To explain these differences, a historical dimension must be mentioned. In the previous five years, no cases of rabies have been reported in Chennai. The Blue Cross of India and other organizations (e.g. Humane Society International) have led very successful campaigns in various Indian cities to capture street dogs, neuter/spay them, immunize them after marking (e.g. ear-notching), and release them back onto the streets. According to the president of Blue Cross (Dr Chinny Krishna, pers. comm.), 'there has been a complete change of human behaviour towards the street dogs since then'. The first author's personal observations over nearly a month of walking the streets of Chennai confirm this. There was an almost complete ignoring of street dogs by pedestrians (even at only 50 cm), or if there was a reaction at all, it was to offer them a bit of food (see Fig. 2.4). Not a single aggressive interaction was observed between the dogs, or between the dogs and people on the streets. Chennai citizens accept



**Fig. 2.2.** Typical scenes during observations in Amman (a), London (b) and Chennai (c). a) One of many well-fed cats sighted in Amman, which occasionally also searched for food in refuse bins; b) dogs appeared to be regularly walked, often by professional dog-walkers, in London; c) One of the many street dogs sighted in Chennai, probably waiting for a piece of cake from one of the tea-house visitors.



Fig. 2.2. Continued.

Country (city)	Total observation time (min)	No. of observation days	Total cats observed	Cats/h observed	Total dogs observed	Dogs/h observed
Jordan (Amman)	747	10	141	11.3	44	3.5
England (London)	673	20	0	0	196	17.5
India (Chennai)	876	12	126	8.6	205	14.0

Table 2.1. Cats and dogs seen per hour of observation in cities of the three countries.

and tolerate (and even look after) the dogs sharing their streets. This is indeed an amazing success story of change for the betterment of human–dog relationships, after combining the efforts of human and veterinary medicine and animal welfare organizations.

## **Concluding Remarks**

It is important to remember that most people worldwide see benefits in keeping companion

animals, and find dogs to be likeable animals; further, that scientific studies have demonstrated those benefits to the health and well-being of people in the general public. However, all peoples of all religions agreed, that if an animal is suffering and cannot be cured, it should be put down humanely. The importance of prevention – through sterilization and immunization, which in the case of Chennai took place – can indeed improve both human and animal health and relations.



Fig. 2.3. Percentage of pedestrians having eye contact with the focal dogs in Jordan (Amman), England (London), and India (Chennai).



Fig. 2.4. The street dogs of Chennai, being spayed/neutered and rabies-free, are either ignored by pedestrians or offered bits of food.

### Notes

<sup>1</sup> For simplicity, the male gender will be used in this text unless otherwise specified.

<sup>2</sup> Japan, China, Singapore, India, UAE, Jordan, Israel, Switzerland, Germany, France, Great Britain and Brazil.

<sup>3</sup> The survey instrument (© D.C. Turner, I.E.T.) may be secured from the first author and used free of charge for other studies under two conditions: (i) no alternations – deletions, additions, or new formulations – may be made to ensure comparability with data from other studies; and (ii) the source of the questionnaire is cited in any publication.

<sup>4</sup> Abdoun Circle in Amman; Bayswater and Kensington Gardens in London; Teynampet, West Mambalam, Triplicane and Guindy Industrial Estate in Chennai.

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# **3** Dog-Associated Problems Affecting Public Health and Community Well-Being

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The chapter will consider problems other than zoonotic diseases affecting public health and community well-being only, and not the adverse effects on the welfare of the dogs themselves. When uncontrolled and uncared for, dogs can be implicated in the transmission of a variety of zoonotic diseases and create other problems or nuisances. Owned dogs that are uncontrolled, or kept in an irresponsible way, are as much a problem as freeroaming, unowned dogs. Despite the hazards due to zoonotic diseases and trauma that may result from the association of humans with dogs, they remain popular pets. In the United States, most owners (60%) own one dog and 28% of owners own two dogs (HSUS, 2011; Westgarth et al., 2008; PFMA, 2008). Fifty three per cent of the households in Sao Paulo, Brazil (Alves et al., 2005), and 17% of households in India (Sudarshan et al., 2006) are reported to own a pet dog. The human-animal bond concept is clearly not restricted to western countries, and is reflected in all cultures throughout the world despite variations in the nature of the human-dog interactions. In this chapter we review a range of issues other than zoonoses associated with dogs, such as injuries to humans and other animals; road accidents; impact on wildlife and the environment, including noise pollution;

and impact on the local economy, particularly tourism. An approximate assessment of the financial cost to the community is given where possible, as well as estimates of the cost of appropriate control schemes. The most complete data are from the United Kingdom and the United States, but comparisons with other countries are given where available. The benefits of the human-dog relationship reviewed in Chapter 2 must be taken into consideration when devising strategies to address these problems. If the incidence of a particular zoonotic disease can be monitored by scientific means, some of the non-disease related problems may be subjective, and their relative importance reflected by differences in cultural attitudes. This will influence the quality and quantity of available data. It is essential to define the problem in the context of the socio-cultural situation in order to offer effective solutions. A total ban on dog keeping, as suggested in the medical literature (Besser, 2007), is both impractical and undesirable.

## Injury to Humans: Trauma and Bites

A 'dog attack' may mean a dog rushing or chasing without any physical contact at all,

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while a bite generally results in the bruising or breaking of skin resulting from contact with the dog's teeth. UK hospital statistics do not differentiate and report on injuries resulting from being 'bitten or struck by a dog'. Accidental injuries from falls can occur with pet dogs and may sometimes reflect a missmatch between the dog (size or boisterous nature) and the carer (a small child or frail older person). Injuries might be avoided by education of potential dog owners to increase awareness and encourage the selection of a dog appropriate for the requirements of the family. Injuries requiring hospital attention following a non-bite incident are often recorded as a fall without mention of a dog, limiting data available. In reality, public safety regulations tend to ambiguously classify dog attacks with bites (Miller and Howell, 2008).

#### Dog-bite data: Effect of source and method of collection

Dog-bite data can be categorized as relating to the victim (race, age, gender, nature and site of injuries, and consequences, etc.), the dog (size, breed, age, gender, health status, hormonal status, social type, consequence, etc.), and the context (geographic location, place, time, season, human-animal interaction, etc.). The data can be obtained from a variety of sources and by different methods, both of which may significantly affect the results. Bias in data on dog and victim characteristics can be observed between different surveys (De Keuster and Butcher, 2008). According to data obtained from hospitals and emergency departments (EDs), the risk is double in children compared to adults (Horisberger, 2002; Kahn et al., 2004; Schalamon et al., 2006). Severe injuries, particularly involving the neck and face, occur most frequently in young children (Kahn et al., 2003; Schalamon et al., 2006). In veterinary caseloads and bite report surveys from non-hospital sources, the relative risk in adults and children appears to be reversed (Guy et al., 2001). The degree of risk, as perceived by the victim, appears to influence the reporting of bites. There is a disproportionate 'over-reporting' of bites inflicted by 'strays', perhaps because

they are thought to cause more disease (Beck, 2000). Cleaveland et al. (2002) used dog bite injury data to estimate the human rabies mortality in the United Republic of Tanzania. In the northern part of Tanzania local communities appeared to successfully recognize when the bite was from a suspect rabid dog (hence a higher risk), and avoided going to hospital for other bites (Cleaveland et al., 2003). People tend to seek medical care and report bites more frequently when bitten by an animal whose owner is not known, as 50% of people bitten by dogs without owners sought medical attention compared to 29% of people bitten by family-owned dogs, and 39% when the dog was owned by a neighbour (Beck and Jones, 1985). It has been suggested that when a child is bitten, owners are more likely to relinquish the dog to a shelter than seek veterinary advice (Guy et al., 2001). A survey by Kahn et al. (2003) found only 24% of the dogs which had bitten a child were presented to a veterinarian.

Dog-bite data will influence the identification of 'risk factors' and facilitate the development of new prevention strategies. It is essential to recognize the importance of the source and nature of data and the potential bias that may be present. The exchange of knowledge between professionals and academics of multiple disciplines is required to better understand what measurements are to be made, how the findings should be interpreted, and how the risk factors deduced.

#### **Incidence of dog bites**

Dog bites in people are a serious public health problem. Each year approximately 4.5 million people are bitten in the United States (representing 1.5% of the total population), with 800,000 bites requiring medical attention and 370,000 bites severe enough to be treated in EDs (CDC, 2010; Gilchrist *et al.*, 2009). Comparable rates are found in Europe with 100,000 people bitten annually in Belgium, equivalent to 1% of the population (Gisle *et al.*, 2001). Figures from the UK's Home and Leisure Accident Surveillance System (HASS/LASS) show that 69,000 people attended hospital Accident and Emergency
departments in 2002 (ROSPA, 2010). In Sri Lanka, the Colombo General Hospital treats approximately 12,000 bite victims per year (WSPA, 2008), and the incidence of bites in India is reported as 1.8% of the population (Sudarshan et al., 2006). However, a number of studies estimate that more than 50% of dog bites remain unreported (Beck and Jones, 1985; Daniels, 1986; Chang et al., 1997; Overall and Love, 2001; Kahn et al., 2004). A survey of 228 veterinary and veterinary nurse students in New Zealand (Wake et al., 2006) indicated that 36% had been bitten in the past, with 20% requiring medical attention, yet only 5% of cases were reported to the authorities. Tan et al. (2004) stress the need for a collaborated approach between local health departments, hospital EDs, and police departments to improve data collection. The true extent of the problem remains difficult to quantify.

#### Costs of bites to health services

Holmquist and Elixhauser (2010) present data from The Health Care Cost and Utilization Project (HCUP) on dog-bite-related ED visits and hospitalizations in the United States. In 2008, about 316,200 ED visits involved a dog bite (equivalent to a rate of 103.9 visits per 100,000 of the population). Approximately 9500 hospital stays resulted from dog bites (equivalent to a rate of 3.1 stays per 100,000 of the population). The average cost of a dog-bite-related hospital stay was \$18,200, which was approximately 50% higher than the average injury-related hospital stay. More than 44% of ED visits and 42.9% of inpatient stays were billed to private insurance. In England in 2008/9, there were 10,563 'finished consultant bed days' resulting from dog bites (The Information Centre for Health and Social Care, 2009/10). The average cost of a 'hospital bed day' is estimated as £317.40, so the cost to the National Health Service (NHS) in 2008 for England can be calculated as £3,352,696. Assuming a corresponding rate for Scotland and Wales, the total cost for Great Britain would be £3,885,650. This does not include the cost of unreported injuries or those that do not lead to a stay in hospital.

#### Victim and site of the bite injury

Data obtained from hospitals and EDs in Europe and the United States indicate children are twice at risk compared to adults (Horisberger, 2002; Kahnetal., 2004; Schalamon et al., 2006; Holmquist and Elixhauser, 2010). Severe injuries, particularly involving the neck and face, occur most frequently in young children (Kahn et al., 2003; Schalamon *et al.*, 2006). In contrast to the belief that facial bites in children correlate with the dog's size, weight, or breed, hospital data indicate a significant correlation between facial bites and the child's age (Kahn et al., 2003; Schalamon et al., 2006). This may be partly explained by the finding that young children explore novel objects, especially those that are mobile, with their face (Meints et al., 2010a). Young children score badly in discriminating dog body language and look mainly at the face of the dog to make their decisions (Lakestani et al., 2005), and very young children may misinterpret a snarling dog for one that is smiling (Meints et al., 2010b). Facial bites in children occur predominantly in the home by a dog that is familiar to the child. Adults are also most often bitten by a familiar dog (Guy et al., 2001), though the site of injury in adults and older children is more commonly the extremities. A study on adult victims (over 16 years) in New Zealand (Wake et al., 2009) reported a bite distribution of legs (45%), hands (35%), and arms (22%). Injuries to the face and hands were more common when the victim was trying to assist an injured dog or interrupt a fight.

Gilchrist *et al.* (2009) estimated that only 20% of bites occur outside the home in public places. Daniels (1986) reported on the incidence of bites on the Navajo reservation. The vast majority of dogs were free-roaming and 42.1% of the victims were children 10 years of age or less, while 71.7% were 25 years old and younger.

Some professionals, such as veterinarians, veterinary nurses, and dog wardens, may be at special risk. It is estimated that 5000 postal workers in the United Kingdom require medical treatment for dog bites every year (Morgan and Palmer, 2007), and a similarly high risk has been highlighted in postal workers in Taiwan (Chen *et al.*, 2000).

#### Bite and dog-associated factors

The factors that determine a dog's tendency to bite have been identified by the American Veterinary Medical Association (AVMA) as heredity, early experience, later socialization, training and education, dog health status, and victim behaviour (AVMA, 2001). These must be considered in the context of human social and cultural factors that have been shown to influence human-dog interactions (Barnes et al., 2006; Messam et al., 2008; Ragatz et al., 2009; Cornelissen and Hopster, 2009). The importance of domestic breeding environments and early socialization are well documented (Appleby et al., 2001). Historically, obedience training and castration have been considered useful to reduce the incidence of bites (Ozanne-Smith et al., 2001). However, in a large study by Reisner et al. (2007), 66% of the dogs involved in bite incidents had previously attended obedience classes and 93% had been neutered. Inappropriate physical punishment and discipline, paradoxically used to reduce aggression, have been identified as trigger factors initiating bites (Herron *et al.*, 2009). Aggression is part of the dog's normal behavioural repertoire, and its expression is largely related to the situation and context. The dog's response to a perceived threatening situation may vary according to the 'ladder of aggression' (Shepherd, 2002). The education of the dog must therefore be of good quality with a full understanding of dog behaviour. The risk of biting may be increased in the presence of pain or disease in the dog (Reisner et al., 2007), and this study also revealed 77% of dogs involved in bite incidents were suffering from an emotional disorder. Rabies is perhaps a special case, not only because 98% of human deaths from rabies are the consequence of a bite from a dog, but also because the presence of the virus in the dog's brain

alters its behaviour, increasing the desire to bite. Cleaveland *et al.* (2002) reported on the use of dog-bite injury data to successfully estimate the human rabies mortality in the United Republic of Tanzania.

Whilst it has been claimed that breedrelated behaviours in dogs are responsible for the majority of bite injuries in children (Shalamon et al., 2006), there is little evidence from dog-bite data to implicate specific breeds as a greater or lesser risk (AVMA, 2001; Overall and Love, 2001; Kahn et al., 2003; Reisner et al., 2007; Cornelissen and Hopster, 2009). Duffy et al. (2008) surveyed the owners of more than 30 breeds of dog using the Canine Behavioural Assessment and Research Questionnaire (C-BARQ). There were significant differences seen among breeds in aggression directed towards strangers, owners, and dogs. Some breeds (e.g. Chihuahuas and Dachshunds) scored higher than average for aggression to both humans and dogs, some breeds (e.g. Akitas and Pit Bull terriers) for dog-directed aggression, and some for human-directed aggression (e.g. Jack Russell Terriers). However, the authors stress that although the results indicate that a propensity to aggressive behaviour is at least partially rooted in genetics, other factors (such as developmental and environmental issues) play a major part in determining whether aggressive behaviour is expressed in the phenotype.

Unfortunately, the majority of victims of serious dog bites and fatalities are young children (Sacks et al., 1996), triggering media exposure focusing on 'aggressive breeds'. As a result, breed-specific legislation has been introduced into many countries despite the fact its efficacy has been questioned (Sacks et al., 2000; Cornelissen and Hopster, 2009; Patronek et al., 2010). Tasker (2007) reports 11 out of 22 European countries surveyed had legislation related to dangerous or aggressive dogs, with some form of breed-specific prohibition. Patronek et al. (2010) used a numberneeded-to-ban calculation to illustrate the limitations of breed-specific legislation in decreasing the risk of dog-bite-related injuries. Their findings indicate the implausibility of such legislation being successful. They consider the enthusiasm for this legislation

is based on misperception of the risk, misinformation and stereotyping, and erroneous beliefs about efficacy. This highlights a so-called perception gap between public fears and the facts. Cornelissen and Hopster (2009) reported on a study in The Netherlands to evaluate the efficacy of breed-specific legislation, and as a result of its recommendations, the Dutch Government repealed its 15-year ban on pit bulls. In the United Kingdom and United States, so-called status dogs are increasingly popular. These are associated with significant problems, though this is largely a reflection of socio-economic difficulties within the community. This issue will be discussed further in relation to injuries to pet dogs. Many such dogs end up in shelters and there is often a desire to assess their suitability for rehoming. A variety of temperament tests may be of use, but few have been scientifically validated and it is recommended they should not be used as the sole means of characterizing a dog (Christensen et al., 2007), especially as they rarely test the temperament in the context of a home situation.

## Context and location of dog bites

The majority of bite accidents in children occur in the home environment and involve young children (median 5 years) bitten by a dog that is familiar to them. In 86% of cases the child– dog interaction that triggered the bite was initiated by the child, and most reported dog bites in children happened while there was no active adult supervision (Kahn *et al.*, 2003).

Bites in a public places generally involve an unfamiliar dog with no prior interaction of the victim acting as a trigger. Over 50% of reported bite incidents in Adelaide, Australia, were from free-roaming and uncontrolled dogs in public places (Thompson, 1997). Territorial behaviour often precedes incidents of dog bites and may be especially prevalent in urban areas where the density of con-specifics is relatively high. While territoriality technically refers to behaviour directed at conspecifics, dogs typically generalize this behaviour to humans that approach or invade the territory (Daniels, 1986). In this study, 47.5% of bite incidents were on a street near the dog's home or primary shelter, while 52.3% were within the private home or yard. The incidence of bites is generally higher in rural areas (Sudarshan *et al.*, 2006; Wake *et al.*, 2006, 2009; Holmquist and Elixhauser, 2010). A questionnaire of 8500 random households in 18 states of India indicated a high incidence (75%) in poor or low income areas, and 63% of bites were inflicted by 'strays' (Sudarshan *et al.*, 2006). Attacks on humans by dogs acting as a pack are uncommon (Kneafsey and Condon, 1995).

Bites can occur when a person is trying to help an injured dog or interrupt a fight. Wake *et al.* (2009) report injuries to face and hands were more common in this situation. Out of 100 incidents involving an attack on a guide dog by another dog, 19% involved an injury inflicted on the handler or member of the public (Brooks *et al.*, 2010).

#### Consequences of bites including fatalities

A Belgian study investigating the follow-up of children treated in EDs for dog bites found that 55% of severely injured children suffered from post-traumatic stress disorder (Peters et al., 2004). Complete data about the circumstances surrounding an attack on children or adults in public places are often lacking. Wake et al. (2009) reported on a questionnaire sent to 1800 adults (aged 16 years or more) who had made claims to the Accident Compensation Corporation in 2002 in New Zealand and had not received serious injuries. Of the 8677 claims made in that time, 72% reported psychological effects, though this may reflect a bias in the population sampled. Dog bites in public places usually happen by surprise, without warning or the interaction of the victim with the dog. It is assumed that this may contribute to a feeling of insecurity in the people being attacked (Kahn et al., 2003; LNV, 2008). Bites occurring in public places often attract media attention, contributing to the perception of dogs being dangerous or unsafe in these situations (LNV, 2008).

Studies in the United States (Sacks *et al.,* 1996), New Zealand (Healy, 1996), and Canada

(Raghavan, 2008) indicate that fatalities from dog bites are rare in the developed world. In The Netherlands approximately one person dies following a dog bite each year. This compares to 11 fatalities resulting from sporting injuries and 23 following household accidents (LNV, 2008). Langley (2009) reported on 504 deaths in the United States from 1979 to 2005. Of the victims, 55.6% were 10 years old or younger, with the highest incidence in infants below 1 year of age. Alaska had the highest death rate. In Canada there are a number of reports of fatalities following attacks by a group of sled dogs (Delise, 2010), which may reflect local management practices. Attacks on humans by dogs acting as a pack, regularly reported in Indian cities, result in severe, sometimes fatal injuries. Unaccompanied children or elderly females appeared especially vulnerable (Kneafsey and Condon, 1995). It has been suggested that hunger, thirst, compromised health status, and feelings of being threatened may increase the risk of pack attacks by 'strays' (Santoro et al., 2010).

## Impact of dog bites/trauma on society and the perception of dogs

A difficult and emotive aspect of public hazard caused by dogs is the fear of dog bites and dog attacks. Although these terms have different meanings, public safety regulations tend to ambiguously classify dog attacks with bites (Miller and Howell, 2008). In Australia, no burden of proof is required to substantiate a dog attack. Councils can declare a dog dangerous with one disputed allegation and impose draconian physical penalties on the dog (such as muzzling, confinement, or euthanasia). Similar rules do not generally exist for other species of pet animals when threatening or harming a human being (Miller and Howell, 2008).

People may be fearful of dogs, especially if they form into free-roaming packs. Alie *et al.* (2005) reported that fear of dogs and having being bitten in the past were two of the reasons people in Dominica would not keep dogs. Bite injuries (personal or to a family member or friend) are very likely to enhance the fear of dogs. Gilchrist *et al.* (2009) estimated only 20% of bites occur in public places. In 51% of these cases the dog was not adequately confined, and in 31% of cases the dog was wandering in the vicinity of its home. Despite the fact that only 20% of dog bites occur outside the private home, the majority of people appear concerned about being bitten by a dog in a public place (LNV, 2008; Cornelissen and Hopster, 2009). This concern influences the legislators, and urban safety regulations (such as leash laws in open spaces and parks) are based on the assumption that these locations are the target areas for people to be chased or attacked by dogs. Miller and Howell (2008) suggest the objectives of public safety can best be targeted by encouraging well-mannered dogs (through exercise and socialization) and that this is achievable through social marketing and collaborative management rather than via the present 'big stick' legal approach of banning dogs in public spaces.

Cleaveland et al. (2003) report on a dog rabies vaccination campaign in rural Africa that dramatically reduced the incidence of dog and human rabies as well as human dogbite injuries. As a consequence, dogs were perceived as safer by the local community, having a positive impact on their interactions with dogs and a subsequent improvement in animal welfare (S. Cleaveland, pers. comm. 2011). This is relevant to the implementation of dog population control programmes. 'Catch/neuter/release' programmes are a component of some dog population control strategies. Free-roaming dogs are captured from the street, vaccinated against rabies, neutered, and then returned to the street. ICAM (2008) stresses the importance of engaging with the community in an attempt to encourage a community responsibility and a subsequent change in human behaviour. The shift to 'collect/neuter/return' and direct involvement of the community could be facilitated if preceded by a mass rabies vaccination programme, reducing the fear of dogs.

#### Assessment of risk posed by a dog

Requests are often made to assess the risk posed by a particular dog. This may be as a

result of national statutory requirements (e.g. legislation and by-laws) or as part of an individual behavioural consultation. A risk assessment is a careful examination of the available evidence relating to potential situations that could cause harm to people or other animals, to determine what measures could or should reasonably be taken to reduce harm. It is not an absolute quantification of risk, but a professional judgment, which informs the advice given. It is unreasonable to expect all risk to be eliminated, but measures should be taken to protect people as far as is reasonably practical. It requires consideration of all relevant physical and behavioural characteristics of the dog, as well as all relevant environmental triggers that may alter either the risks associated with any injury, or the risk of recurrence. The European Society for Veterinary Clinical Ethology has produced a Position Statement on Risk Assessment (ESVCE, 2011) which provides a framework as a model of good practice.

The risk assessment of a dog in a well-defined situation identifies five stages:

**1.** assess the proposed circumstances (risk factors);

**2.** identify the hazards (how individuals may be harmed);

**3.** decide who might be harmed or at risk, identifying individuals or groups who are at most risk;

**4.** evaluate the risks and decide on precautions, considering the risks in terms of their nature, probability, and severity;

5. record the findings and implement them; and

**6.** review the assessment and update as necessary.

The dog-bite related factors to consider in evaluating the risk following an aggressive incident towards familiar people and animals, as well as dog behavioural features which alter the general risk of recurrence are summarized by De Keuster and Jung (2009). Factors influencing the prognosis for treatment, should it be considered desirable, are also discussed. Differential diagnoses and characteristics of aggression towards unfamiliar people and animals are considered by Bain (2009).

#### **Dog-bite prevention programmes**

Understanding the context of the bite is essential in developing prevention programmes. Data on dog/child interactions have been published in the veterinary and medical literature, and 'Prevent a Bite' programmes established in schools and health care centres. Most of these are aimed at children older than 7 years and focus on public safety rules, such as how to behave when encountering an unfamiliar dog (Chapman *et al.*, 2000). They traditionally attempt to teach how to recognize the dog's body language. However, young children score badly in discriminating dog body language and look mainly at the face of the dog to make their decisions (Lakestani et al., 2005). Young children will often confuse a frightening with a friendly dog (Love and Overall, 2001; Meints et al., 2010b). Programmes intended to prevent bite accidents in the home are rare, and the Blue Dog was developed specifically to fill this gap. It was designed by a team of professionals from multiple disciplines to target the main at-risk group (i.e. children below 7 years of age) in the context of the home. It takes the form of an interactive CD-ROM and printed parent guide, and focuses on teaching parents and children to recognize potential risk situations that trigger dog bites in everyday household situations (De Keuster et al., 2005). These include resource guarding (such as food, bones, and toys) or interactions (such as petting, hugging, or kissing). To make the programme attractive to children, the educational messages are wrapped in an entertaining context, thus transforming the prevention-only screenplay into an 'edutainment' tool. A scientific assessment of the programme showed that children of the target age group learnt from the Blue Dog scenes, and that parental input enhanced the performance of the child and improved the ability to retain the acquired knowledge (Meints and De Keuster, 2009).

The educational message and tools used must be suitable for the particular context. A collaborative project involving the World Society for the Protection of Animals (WSPA), the Blue Paw Trust Sri Lanka, and the Colombo Municipal Council (CMC) includes a junior school dog-bite prevention programme using puppet shows, songs, and posters (WSPA, 2008).

#### Injury to Livestock

Accurate information on the extent and cost of dog attacks on livestock is lacking. In 1978 the UK government reported that 8000 animals were killed or injured by dog attacks, but no further records were kept after this time. The RSPCA and Kennel Club (1998) quote data sourced from the National Farmers' Union Mutual Insurance Society which were limited to dog attacks on (insured) sheep. During the period 1993–1996, the total number of sheep injured each year varied from 13,500 to 21,000, at an annual cost to the farmer of between £1.2 million and £1.7 million. Allowing for inflation, the RSPCA (2010a) estimate the total cost of injuries to livestock resulting from dog attacks in the United Kingdom in 2009 to be valued at £2.8 million. The killing of chickens by dogs was reported in a household survey conducted in Soweto, South Africa (McCrindle et al., 1998).

#### Injury to Pets

The extent of attacks by dogs on other dogs is difficult to ascertain. The RSPCA (Harmsworth Memorial) Animal Hospital provides a charity service in an inner-city area of London. Their clinical records indicate that 258 dogs were presented suffering bite wounds in 2010, representing 1.4% of the first consultation caseload (D. Grant, pers. comm. 2011). This compares to an incidence of 2.3% of first consultations seen during the same period in a private veterinary hospital in a suburban area of London (K.E. Beasley, clinical records from the Wylie Veterinary Centre, pers. comm.). The survey of Duffy et al. (2008) has been discussed above and indicates that some breeds (e.g. Akitas and Pit Bull terriers) may show a propensity for dog-directed aggression compared to human-directed aggression. This is interesting in relation to the increasing popularity of status dogs seen in the United States

and United Kingdom. The RSPCA (2010b) highlights an increasing problem of antisocial behaviour where dogs are used in an aggressive or intimidating way towards the public or other animals. This often, though not exclusively, involves young people on inner-city estates and may involve subjecting the dogs to fights. The RSPCA received 358 calls specifically about dog-fighting in 2007, compared with 137 in 2006 and 24 in 2004. The Metropolitan Police of London seized 1152 dogs under the Dangerous Dogs Act (1991) in 2009/10, compared to 173 in 2006/7 (Grant, 2011). Those reprimanded have sometimes been shown to be involved in criminal activity, and the concern has been expressed that impromptu dog-fighting could become more organized and involve gambling. Sadly, this use of such dogs is a reflection of innercity poverty and wider socio-economic problems highlighted by Marmot (2010). This has an implication for the enforcement of legislation. Grant (2011) questions, 'How do you enforce dog laws with a group of individuals who are completely outside the law and who have no respect for any authority except that of the gang, and who seem to lack empathy with the dogs they own?' There is evidence of a correlation between ownership of high-risk dogs (licensed or cited) and the presence of deviant behaviours in the owner as indicated by court convictions. It is suggested that the ownership of a high risk ('vicious') dog can be a significant marker for general deviance and should be an element considered when assessing risk for child endangerment (Barnes et al., 2006). Ragatz et al. (2009) found a significant difference in criminal behaviour based on the types of dog owned. Owners of vicious dogs were significantly more likely to admit to violent behaviour compared to owners of other types of dog.

Brooks *et al.* (2010) report 100 incidents of attacks on guide dogs by another dog between 2006 and 2009. In 61% of cases the guide dog was working in harness. Most attacks occurred in public places and in 61% of the cases the attacking dog was off the lead at the time of the attack. A dog of the 'bull breeds type' was the aggressor in 45.7% of the incidents, which was an over-representation compared with an estimated proportion in the national population (5.9%). Veterinary attention was required following 41% of the attacks. The working performance and behaviour of the victim was affected in 45% of cases, and 2 of the dogs were subsequently withdrawn from service. It is estimated that each guide dog has a lifetime cost of approximately £50,000, so any injuries that affect the dog's ability to work have a big potential cost impact, as well as causing logistical and psychological difficulties for the blind person. It was reported that the owner of the aggressor apologized to the victim's handler in only 6% of the cases, and this may reflect the status dog culture discussed above. Brooks et al. (2010) further note that only 16% of the attacks were reported to the police and 2% to the local dog warden. Of those reported to the police, only 31.3% progressed to charges being made and a subsequent prosecution.

Catch/neuter/release programmes are sometimes a component of a dog population control strategy. Financial or logistical constraints often mean that bitches are targeted in preference to males. It is possible that a larger number of un-neutered male dogs competing for a relatively smaller number of females in oestrus might result in an increase in dog–dog aggression at these times.

## Road Traffic Accidents Caused by Dogs

Until 2004, the UK's Department of Transport recorded the number of road traffic accidents caused by dogs involving a human casualty. Records of accidents without a human casualty were not kept. In 2004, one human fatality, 32 serious accidents, and 254 slight accidents were reported, continuing a steady decline seen over the previous decade. Ganeshan (2008) valued these accidents according to accepted economic valuation (i.e. £1,906,200 for a fatality; £218,100 for a serious accident; £22,600 for a slight accident). It was further assumed that if the data were to apply to 2008/9, the resultant cost underestimates would be balanced by the continuing decline in numbers of accidents, giving an overall estimated cost for 2008 in Britain of £14.6 million.

However, such figures are difficult to interpret, as the presence of the dog is only one of many variables that will affect the severity of the injury and hence the cost. Road traffic accidents are a major cause of death and injury throughout the world. The WHO (World Health Organization) Regional Office for Europe (2009) reports an annual total of 120,000 human deaths, 2.4 million injuries, and a cost of approximately 3% of the GDP. Stricter controls on drink driving, speeding, the use of seat belts and child restraints, and the wearing of helmets for users of motorized two-wheelers are recommended. Worldwide, the problem is worse in lower-income countries (WHO, 2009).

#### Impact on Wildlife

This is important, though may not necessarily be considered as a public health issue. There is, however, a 'cost' to the community and the ecosystem which might influence public opinion and give added pressure to introduce dog control measures. Feral and semi-feral dogs have been reported to prey on capybaras (Hydrochoerus hidrochaeris) in Venezuela (MacDonald, 1981), and populations of endemic fauna on the Galapagos Islands (such as giant tortoises, marine iguanas, flightless cormorants, and blue-footed boobies) are seriously threatened by feral dogs (Barnett and Rudd, 1983). A more complete consideration of the impact of dog populations, including the interbreeding with native species of Canidae, is given in Matter and Daniels (2000). Removing all the dogs from an environment, as is sometimes suggested as a control measure, will result in food resources being available to other species which may have an impact on the ecosystem.

## Pollution from Faeces, Urine, and Tearing Open Garbage

The fouling of public parks and open spaces is one of the major grievances among the nondog-owning population against dog owners (RSPCA and Kennel Club, 1998). Horn *et al.*  (1990) reported more than 60% of children's playgrounds in Hanover were contaminated with parasite eggs (mainly Toxocara spp.). It has been reported that in Paris, 150,000 dogs produce 16 tonnes of faeces per day (Brandow, 2008). Faecal contamination was one of the problem areas highlighted in a household survey conducted in Soweto, South Africa (McCrindle et al., 1998). Alie et al. (2005) cited the mess produced by dogs as one reason given for people not keeping dogs in The Bahamas. As well as the zoonotic and aesthetic problems, it has been suggested that the large volume of dog faeces and urine produced could have a significant impact on the pollution of waterways due to the associated excess nitrogen (Watson, 2002), though the relative effect may be small compared to human sewage and the run-off from agricultural activities.

The problem of faecal pollution became a major political issue in many major cities in the 1970s. Brandow (2008) traces the history of New York's 'Poop scoop' legislation, highlighting the significant barriers in public opinion that were overcome before the law was enacted and subsequent enforcement made it a success. Initially many politicians thought the idea absurd, and animal rights activists were unanimously opposed on the grounds that it would impose undue hardship on dog owners. Brandow (2008) also reviews the alternative approaches that have been tried, notably in France. Specially designed motor cycles with vacuum cleaners ('moto-crottes') were introduced, but these proved to be expensive and ineffective, and were phased out in 2005. Sand boxes ('canisettes') have been installed in a number of cities in France with minimal effect. In the event, the 'poop-scoop' approach proved to be the most successful and was copied in many other cities throughout the world. In the United Kingdom, the Dog (Fouling of Land) Act in 1996 and Clean Neighbourhoods and Environment Act (2005) make provisions that empower local authorities to initiate 'poopscoop' programmes and on-the-spot penalties for violators. Brandow (2008) suggests that the success of the 'poop-scoop' legislation was dependent on the fact that it stimulated a modification in the behaviour of dog owners

and an acceptance by society that this serious issue could be addressed in this way.

Respondents to a household survey conducted in Soweto, South Africa, cited tearing open rubbish as one of the dog-related problems in their community (McCrindle et al., 1998). Food mixed in garbage is a natural resource for free-roaming dogs, and in part explains why high population densities can be maintained. Improved garbage control is a solution and is generally achieved in higher-income neighbourhoods. As a general rule, straying pets are more common in high human density, low-to-middle-income areas, especially where people have direct access to the streets. Ownerless strays are more common in low-density, low-income areas where there is shelter and few requests for animal control, such as around parks, dumps, or abandoned parts of the inner city (Beck, 1973). Targeted garbage control may be useful to discourage free-roaming dogs in specific areas such as markets or children's play areas. In some communities the eating of refuse (and human faeces) may be regarded as a positive cleaning function performed by dogs that is welcomed (WHO/ WSPA, 1990).

#### Impact of Noise

Vocalization in dogs is common and may be due to outside stimuli, social facilitation with other dogs, territorial displays, or play (Horwitz, 2009). It is also one of a range of separation-related behaviour problems that may occur in the partial or complete absence of the pet's owner. These problems can have different underlying motivations, relating to factors such as fear, anxiety, over-attachment, and lack of appropriate stimulation, and require different treatment interventions (Horwitz, 2009). If not corrected this can put a strain on the human-animal bond, and is cited as one of the higher-risk factors for relinquishing dogs to shelters (Patronek et al., 1996). Alie et al. (2005) cited noise as one of the reasons that would discourage people from keeping dogs in Dominica, and noise was considered to be a nuisance

reported in a survey carried out in Soweto, South Africa (McCrindle *et al.*, 1998).

In the United Kingdom, the control of noise pollution is governed by the Environmental Protection Act (1990). According to case law, a statutory nuisance is regarded as a 'material interference with the comfort and enjoyment of another's home'. Complaints about dog barking are dealt with by the environmental health department of the local council. St Helens Council, United Kingdom (2010) reported that of all neighbourhood noise complaints, barking dogs are the most numerous, accounting for approximately 30% of cases. The local authority of Okanagan Lake, British Columbia, Canada, (Okanagan Lake British Columbia Local Authority, 2010) reports 417 complaints relating to barking dogs in 2010 (representing 18% of total complaints about dogs), while that of Wanganui, New Zealand, reported 403 cases in 2007/8 (representing 15%) of total complaints about dogs) (Wanganui Local Council, 2008). Many municipalities have websites giving information about what to do if exposed to excessive barking, and so this is clearly a widespread problem.

Many dogs (65%) in Roseau, Dominica, are used for security purposes (Alie *et al.*, 2005). Some are referred to as 'watch dogs' and these are generally encouraged to bark as a warning, but not to attack an intruder. The dog's function is therefore to bark, and so the resulting noise may contribute to the nuisance perceived by others.

#### Impact on Local Economy

The presence of free-roaming dogs may have a negative impact in countries dependent on a tourist industry. Fielding and Plumridge (2005) note that tourists may be upset by seeing 'potcakes' (local mongrel dogs) roaming the street on New Providence, The Bahamas. Ross and Mirowsky (1999) further suggest that the presence of free-roaming dogs may project an image of inner-city decay, drugs, and violence – all of which is detrimental to a tourist-based economy.

Brandow (2008) suggests that the level of dog faecal pollution experienced in New York

in the 1970s was sufficient to alarm politicians of the possibility of businesses relocating to other cities, thus having a significant potential economic impact.

#### **General Cost of Control Schemes**

Many of the problems discussed above can be addressed, at least in part, by promoting responsible pet ownership both at the individual and at the community level. This requires education that results in a change in the behaviour of people. The ICAM (2008) Humane Dog Population Management Guidance stresses the need to tailor the dog control strategy to the specific local situation. The components of the strategy may include legislation, registration and identification, control of reproduction by neutering, control of breeders and sales outlets, garbage control, and education. An overall strategy would include more than one of these components, though it should prioritize the most costeffective ones for the particular situation. All components of the strategy should be aimed at changing people's behaviour.

Within mainland Europe, Tasker (2007) has identified 23 countries with a dog licence and registration scheme. In Slovenia and The Netherlands dog control provisions have improved, with low numbers of stray dogs, and compliancerates of more than 50% (Upton et al., 2010). The Slovenian situation is described as well controlled, containable, and sustainable, and many of the municipalities have adopted 'leash laws' prohibiting the loose running of owned dogs in public areas. Compliance is improved by the favourable attitudes of the general population. In Germany there is a national dog registration scheme but this is implemented at the local level. It is reported that the standard of responsible dog ownership is high, with shelters working at undercapacity, providing financial savings for local authorities and NGOs (non-government organizations). Switzerland also has an efficient system with good compliance. These findings are consistent with the findings of Turner and Waiblinger discussed above (D.C. Turner and E. Waiblinger, pers. comm. 2011).

Pescara is said to have one of the most successful registration and identification schemes in Italy, with a compliance of 70% as compared to 30% for the rest of the country. This has resulted in a reduction in strays from about 5000 dogs in 2004 to 2300 in 2008, as well as an improvement in responsible pet ownership. It is reported that there has been a reduction in uncontrolled reproduction, a reduced risk to humans of zoonoses, a reduced level of environmental contamination, and an improved control of activities such as dog-fighting (Upton *et al.*, 2010).

Compulsory identification and registration has been in place in Victoria, Australia, since 1970. Compliance is reported to be about 64%, though this varies between urban and rural areas. Reported benefits include a reduction in the number of free-roaming dogs, reduced environmental contamination, a decreased risk of zoonoses, and an improved control of activities such as dog-fighting (McMurray, 2005). The improved level of responsible pet ownership has also resulted in a decrease in the number of complaints about dogs: 10% of the pet population is involved in animal complaints, compared to 20% prior to introduction of the legislation. There is evidence that a pilot scheme to achieve humane and sustainable dog population control in Colombo, Sri Lanka (WSPA, 2010), is achieving a significant reduction in the number of dog-related complaints received by the Colombo Municipal Council (CMC).

Alie et al. (2005) report that dog licensing is in place in Roseau, Dominica, but there is poor compliance. This is thought to be in part due to widespread ignorance of the law, stressing the need to implement public education programmes. Interestingly, their survey showed that respondents from households without dogs thought that the registration fee should be approximately four times higher than those from dog-keeping households. This may reflect a desire to make it difficult for people to keep dogs, or perhaps the feeling of non-dog carers that dogs are a nuisance and their carers should be penalized. The lower fee suggested by the dog carers probably reflects their opinion that they should be free to exercise their 'right' to keep a dog. In reality a compromise often has to be reached,

and ICAM (2008) stresses the need to take account of the opinions of all stakeholders.

In 2008, a pilot rabies control project was initiated in the Visayas archipelago in the Philippines, focusing on eliminating rabies from the reservoir species (the dog) using humane methods. This was based on the Philippines' National Rabies Prevention and Control Program (NRPCP), which included the provision for compulsory dog registration according to the Anti-Rabies Act (2007). Overall, the preliminary results of the programme are very encouraging. However, though the introduction of registration is to be applauded, the fees and penalties imposed were viewed by some to be high relative to the local economy, such that it could potentially reduce compliance and encourage abandonment. This could be counterproductive to the medium-term aim of encouraging responsible pet ownership, and highlights the importance of ensuring that all the fine details of any plan are appropriate to the local situation.

Registration and identification are two of the key components to promote responsible pet ownership. Despite this, mandatory dog licensing was abolished in Britain in 1987, and microchip identification is currently voluntary. The funding of rehoming and educational initiatives is largely the responsibility of charities and NGOs. In addition, the RSPCA is responsible for 80% of the prosecutions under the Animal Welfare Act (2006), and they estimate the total costs associated with these activities to be in excess of £50 million in 2009 (RSPCA, 2009a). Local authorities are obliged to keep stray dogs for 7 days, after which many are passed to charities for rehoming. Approximately 42-46% of stray dogs collected were returned to their owners (RSPCA, 2009b; Dogs Trust, 2009). The average length of stay in kennels run by the major UK charities is 30.5 days at an average cost of £7.54 per day (RSPCA, 2010a). It is suggested that mandatory registration and identification would speed up the rehoming, with annual savings in kennel costs estimated between £2.8 million and £7.5 million. In addition, the resulting increase in kennel capacity would further reduce the requirement for euthanasia of healthy dogs. There are an estimated 10,500 registered animal NGOs within the

United States, with a total annual expenditure of US\$1,902,380,623 (A. Rowan, pers. comm. 2010). In addition, the Municipal Animal Control entities have an estimated budget of \$1,068,225,000, leading to a total annual expenditure on animal protection and animal control of approximately \$2,970,605,623.

The local authorities within the United Kingdom fund dog wardens who have a statutory responsibility to ensure compliance with local dog control orders, as well as dealing with stray dogs, dangerous dogs, and complaints from the public. There is considerable variation between councils (especially between rural and urban areas), and the average recorded cost of a dog warden service is £112,715 (Upton et al., 2010). Given that there are 408 local councils, the total cost to the United Kingdom is estimated to be approximately £46 million. The RSPCA (2010a) has calculated the total cost of running a properly funded registration scheme in the United Kingdom to be a minimum of £107 million. Assuming 75% compliance and a total population of 10 million dogs (Murray et al., 2010), this would equate to an annual dog licensing fee of £14.30 per dog; at 50% compliance the cost would increase to £21.50 per dog.

A report in the Cape Town News (2009) indicated that 400 complaints were logged daily by the police department, of which 100 relate to dogs (70% of these relate to barking and making a nuisance). It was calculated that dealing with dog complaints cost R50,000 per month, which represented a large drain on resources and manpower.

#### **Education is the Key**

Alie *et al.* (2005) report on a preliminary survey of 300 households carried out by Roseau City Council, Dominica, in collaboration with the International fund for Animal Welfare (IFAW). They found that 90% of respondents agreed there was a roaming dog problem and that education was the key. However, this posed a difficulty, as relatively few dog carers visited the veterinarian, so novel ways of reaching the average carer needed to be developed. Carers were described generally as 'passive' and the aim was to educate them to become more 'active' through increased interaction with their pets, benefiting both pet and carer, reducing the presence of dogs on the street, and thereby the problems caused. A collaborative project to achieve humane and sustainable dog population control in Colombo, Sri Lanka, has a broad spectrum of activities that includes education in dog-bite prevention. By 2010, significant progress had been achieved (WSPA, 2010), reaching 54,582 primary school children, 19,836 secondary-school children, and 4171 members of the community. Puppet shows have been used successfully in low-income government primary schools. Pre- and post-education evaluation (of five key bite messages) indicated students learnt the message following the initial lesson and that there was significant knowledge retention after 6 months. The community education programmes involved the use of street drama and DVD lectures. These were found to be more effective in the evenings, as this was when more people attended and there was a better spread of age and gender. There is anecdotal evidence of a reduction in the number of dog bites in children, and a full analysis of the data is in progress.

Research has shown that a reduction in the incidence of in-home injuries in young children is not related to their knowledge of home safety rules, but rather to their compliance and to the extent of parental supervision (Morrongiello et al., 2001). Similar findings were found in relation to the prevention of road traffic accidents in children (Zeedyk et al., 2001). Physical proximity was the only aspect of parental supervision behaviour that served a protective function (Morrongiello and House, 2004). The development of the Blue Dog programme incorporated these lessons (De Keuster et al., 2005), but has also highlighted other important issues (De Keuster and Butcher, 2011). Difficulties have been experienced in promoting dog-bite prevention messages. The strategy initially involved a 'fear' message (every dog has the potential to bite). An important pitfall is to assume that health prevention campaigns will necessarily induce a danger-control process, which in turn will cause a change in behaviour (Witte, 1993). Messages designed to scare people by

describing the terrible things that will happen to them if they do not do what the message recommends may induce a fear response with subsequent message rejection. This requires careful consideration of how to balance a 'fear' message with a 'feel-good' one.

#### Conclusions

Many studies have shown the human-dog bond has a positive impact on human health, child development, and the quality of life. However, there are problems, and the challenge is to devise strategies that allow us to live safely with dogs so we can retain the benefits yet reduce the risks. It is recognized that the complexities and contradictions of human-dog interactions result in tensions (Leney and Remfry, 2000). These result in real issues, but there are also real solutions, and controlling the conflicts between the owner's expectations and the dog's nature is one of the important challenges in public health and animal welfare (Beck, 2000).

Reducing the nuisance of free-roaming or uncontrolled dogs in public places requires a comprehensive dog population management programme that takes account of all stakeholders. The considerable costs involved must be balanced against the economic savings achieved in specific areas and the improvements in community well-being. Legislation (including registration and identification) has an important role to play, but will be most effective if the provisions and penalties reflect what the local community consider right and proper. These measures should be regarded as an opportunity for public education, as it is only by changing people's behaviour that the problems will be resolved. In this regard, the New Zealand Animal Welfare Act (1999) and the UK's Animal Welfare Act (2006) are good examples as they introduce the concept of a 'duty of care' with the provision to incorporate accepted codes of practice (Animal Welfare (Dogs) Codes of Welfare, 2010). Issues related to status dogs may be more problematic as those responsible may act outside the law and have little respect for authority. Tackling the underlying socio-economic problems of inner

cities is essential (Grant, 2011). It is important that the human–dog bond is taken into consideration when planning towns and cities. Urban animal management rules need to be devised that protect people from the perceived dangers of dogs while allowing dog owners to enjoy the benefits (Miller and Howell, 2008).

Problems within the home environment cannot easily be addressed by legislation. Barking in pet dogs as a result of separation anxiety requires veterinary or specialist behavioural advice. Bites to children in this context can generally be regarded as 'accidents in the home' that can only be reduced by parents providing a safe home environment with adequate child supervision. This requires an understanding of child behaviour as well as dog behaviour.

Effective strategic decisions on prevention require the correct interpretation of good data. Consideration of the available dog-bite data highlights the importance of recognizing the source and nature of data and the potential bias that may be present. It is essential to exchange knowledge between the various professions involved (e.g. veterinarians, physicians, policemen, dog catchers, etc.) and academics, in order to better understand what we are trying to measure, how we should interpret the findings, and how we recognize the risk factors.

Education remains the key. It is important to agree the correct message, identify the target population, and decide on the best group(s) to present the message. The educational tools selected must be appropriate for the culture, age, and abilities of those to be educated. The message must be presented in a balanced way. Witte et al. (2001) stress that effective health-risk messages need to stimulate a cognitive response in the target audience in order to modify their behaviour, yet avoid a fear response that leads to message rejection. The perception gap between public fears and the facts may lead to misperception of the risk, misinformation, and stereotyping, and erroneous beliefs about efficacy of proposed control measures (Patronek et al., 2010). Finally, it is essential to monitor the efficacy of the education programme – not simply whether people learn and retain knowledge, but that their behaviour is modified in an appropriate way that achieves measurable benefits.

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# **4** Dogs and Rabies

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Rabies is a one of a variety of zoonoses in a number of mammalian hosts, each caused by a distinct Lyssavirus variant. It has been recognized since antiquity as a disease entity with characteristic clinical and epidemiological features. However, its ranking among all human health concerns is difficult. Recent efforts of its ranking among other neglected tropical diseases including zoonoses using disabilityadjusted life year (DALY) estimates give it a fair position (Knobel et al., 2005). With 1.7 million DALYs rabies comes close to leishmaniasis, in front of trypanosomiasis and leprosy, but far behind soil-transmitted helminthiases and lymphatic filariasis. It is a reportable disease in many countries, and many countries also provide legislation for controlling it, though this is rarely enforced. Rabies control programmes aim at protecting human health and preventing economic losses. The occurrence of rabies in humans can be controlled by pre- and post-exposure prophylactic vaccination and by reducing the risk of exposure, or conclusively, by disease elimination in the host species. The most cost-effective way to reduce the incidence of human infection is by prophylactic immunization of those domestic animals which are the most common source of human exposure, such as the dog. It is a considerably more ambitious task to eliminate

rabies in its principal host populations, which may be impossible to date in many wildlife species, particularly in bats.

Although most mammalian species are susceptible to infection with rabies viruses, only a few are recognized as important for the persistence of the disease in nature. In these principal host species, a prolonged enzootic existence is possible because of sets of coadapted traits of susceptibility, viral evasion of immune surveillance, long incubation, excretion in saliva, neurological disorders that promote transmission, host life history traits, social behaviour, and population biology. Chiroptera (bats) are identified as hosts of lyssaviruses in Africa, the Americas, Australia, and Eurasia. Different species of Carnivora, including the domestic dog, are the principal hosts for classical rabies (serotype/genotype 1) in Africa, the Americas, and Eurasia. From a practical human health and disease control standpoint one may distinguish between bat rabies, rabies maintained by wild carnivores, and dog rabies.

## **The Rabies Virus**

Rabies virus and related viruses constitute the genus *Lyssavirus* (Tordo *et al.*, 2005). Lyssaviruses are members of the family

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*Rhabdoviridae* (Greek *rhabdos* = rod) and of the order *Mononegavirales*. All rhabdoviruses share a common morphology, genome structure, and replication mechanisms (Tordo *et al.*, 2005).

#### **Rabies Virus Structure**

The rabies virus genome is an unsegmented negative strand RNA molecule of approximately 12,000 nucleotides in length, coding for the five rabies virus structural proteins designated N, P (formerly M1 or NS), M (formerly M2), G, and L (Tordo, 1996). Rabies viruses are enveloped short cylindrical rods of approximately 75 nm in diameter and 100-300 nm in length. They are often described as bullet-shaped, rounded at one end, and more or less flat at the other. The virion envelope is composed of membrane (matrix) protein (M) and glycoprotein (G-protein) molecules, the G-protein forming spikes that cover the surface. Inside the virion is a dense helical ribonucleocapsid cylinder consisting of the viral genome RNA covered with N, P, and L-protein molecules. The large L-protein functions as virion-associated polymerase.

#### Virus Replication

Rabies virions bind to cell surface receptors with the assistance of specific regions of the G-protein. One of these binding sites is the nicotinic acetylcholine receptor (Baer and Lentz, 1991). Other receptors may also be important, but they are not yet well characterized. Bound virions are internalized into endosomes, from where the ribonucleoprotein (RNP) complexes are released into the cytoplasm. The genomic negative-strand rabies RNA is transcribed into positive-strand 'antigenome' for replication and messenger RNAs for protein synthesis (Tordo and Kouznetzoff, 1993). The newly made G-proteins are incorporated into the host cell membrane, while the other synthesized viral proteins encapsidate the RNA progeny to form RNP. RNP accumulates in inclusion bodies, which are visible in histological preparations as Negri bodies. RNP strands are coiled into dense

helices before they are incorporated into virions budding from cellular membranes fitted with G-protein spikes.

#### Physical Properties

Rabies viruses are quite fragile. They are readily inactivated by elevated temperatures, UV light, detergents and organic solvents, and by extreme pH values. The destructive influence of physical and chemical agents is greatly modified by stabilizing effects of polypeptides and other compounds (Michalski *et al.*, 1976). This signifies in practical terms that most of the virus on the exposed surface of a dead animal is inactivated within a few hours, and that the infectivity in internal organs is lost within a few days in summer, but can persist for many weeks under cool weather conditions.

#### **Other Lyssaviruses**

The lyssaviruses are a distinct genus within the Rhabdovirus family, which currently contains seven species (genotypes), with a further five proposed types. All lyssavirus isolates have been isolated from mammals, with most viral types being maintained by various species of bats. Viruses of all genotypes cause rabieslike clinical disease in mammals. Genotype 1 is the 'classical rabies' type, which includes dog rabies variants. Genotypes 2 (Lagos bat virus), 3 (Mokola virus), and 4 (Duvenhage virus) are confined to Africa. Genotypes 5 and 6 (European bat lyssaviruses 1 and 2) are restricted to Europe (Eurosiberia), while genotype 7 (Australian bat lyssavirus, ABLV) occurs in Australia. Further proposed genotypes currently consist of single isolates from Eurasian and African bats (Botvinkin et al., 2003; Kuzmin et al., 2003, 2010).

## **Antigenic and Genetic Variation**

The mutation rate of RNA virus genomes is a thousand- to a million-fold higher than that of DNA genomes. This is due largely to the absence of intrinsic proofreading mechanisms in RNA replication. Average frequencies of base substitutions in rhabdoviruses are estimated to be  $10^{-4}$  to  $4 \times 10^{-4}$  per base incorporated. Such a level of base change dictates that RNA viruses exist as heterogeneous populations. The expression 'quasispecies' is frequently applied to such polymorphic populations. However, it should be noted that the predictions from a mathematical model describing populations of self-replicating RNA molecules characterized by a high rate of erroneous copying are only partially fulfilled. Despite the obvious potential for random viral mutation, overall high levels of conservation are found in wild rabies isolates. This suggests that substantial selective pressures do operate. The quasispecies concept highlights the evolutionary potential of genetic variation. A polynucleotide can guide itself along fitness gradients to fitness peaks. If 'self-guided tours' in the fitness landscape were a possibility for rabies virus, one would expect that it should switch principal hosts opportunistically. This is obviously not the case; rabies genomes appear to be trapped at local fitness optima. Adaptations to new hosts or the adoption of other transmission strategies may both be difficult due to structural and functional constraints, or may need too many simultaneous co-adapted changes. Though intricate, future invasions of new hosts are possible at a similar frequency as they have occurred in the past.

Despite the obvious constraints on random variability, hosts do permit some viral polymorphism. Such heterogeneities have been described in individual hosts (Morimoto *et al.*, 1998) as well as in host populations (Nadin-Davis *et al.*, 1993). Molecular genome analysis is necessarily more apt to uncover polymorphism than phenotypic analysis with monoclonal antibodies (Mabs). There are essentially two reasons for this: more mutants are synonymous than non-synonymous, and a fair number of non-synonymous mutants are not detected by Mabs, both indicating functional constraints on the phenotypic structure.

The viral polymorphism poses some diagnostic challenges, particularly when examining individual infected hosts. Neither molecular analysis of a PCR product with REA (restriction enzyme analysis), nor consensus sequencing, nor the application of Mabs for a phenotypic examination will necessarily detect viral heterogeneity. In the best case these methods detect one of several variants present; in the worst, they let a mixture of variants appear as a new version of the virus.

#### Virus variants occurring in dogs

In Europe and North America dogs are frequently infected with the rabies virus variants circulating in populations of wild Carnivora, such as red foxes, striped skunks, and raccoons. Only rarely are dogs infected with American bat rabies variants. All these cases are considered spillover from a host that permits a particular virus variant to enzootic persistence, to dogs, a species that is susceptible, but does not have the appropriate biological attributes for continuous transmission of this virus in its populations. The situation is rather more complicated in Southern Africa, where rabies epizootics in dogs and in jackals (Canis mesomelas and C. adustus) appear to be independent, though caused by identical virus variants (King et al., 1994; Bingham et al., 1999; Zulu et al., 2009).

Virus variants from areas with predominant dog rabies are all very similar when analysed with monoclonal antibodies (Wandeler, 1991a). This may indicate functional constraints in their adaptation to the species, but more likely it is reflecting a common ancestry. Smith et al. (1992) have analysed the genetic relatedness of rabies virus isolates using N-gene sequence data. It is quite striking that isolates made from rabid dogs from Africa, the Americas, Asia, and Europe are all genetically related and form the so-called 'cosmopolitan lineage' (see also Nadin-Davis and Bingham, 2004). This lineage also includes the European fox rabies virus and isolates from wild Carnivora in Africa. The authors concluded that the similarity of many dog rabies virus variants from around the world is most likely the result of the introduction of European dogs and their viruses in colonial

periods. It should be kept in mind that episodes of anthropogenic spread of rabies with dogs could also have occurred at pre-colonial, if not prehistoric, times.

### Pathogenesis

Rabies has a peculiar pathogenesis that is characterized by virus dissemination within nerve fibres rather than by blood and lymph, the rapid expansion of the infection within the CNS after a variable, but generally long incubation period, virus excretion with saliva toward the end of the incubation period, and the almost invariably fatal outcome.

## Transmission

Rabies virus is normally transmitted from dog to dog with virus-laden saliva of the diseased animal via bite wounds. Non-bite transmission (ingestion, inhalation, and other mucosal exposure) has been occasionally implicated. It has been suggested that infection may result from mouth-licking and through consumption of regurgitated food, both common practices in many social canids. Such forms of transmission may have occurred in outbreaks which have decimated packs of African painted dogs (*Lycaon pictus*) (Kat *et al.*, 1996; Hofmeyr *et al.*, 2000, 2004).

#### Susceptibility

Dogs were not very susceptible to a European fox virus in experiments conducted by Blancou (1985). The  $LD_{50}$  (dose required to kill 50% of the animals inoculated) for dogs inoculated intramuscularly was between  $10^5$  and  $10^6$  mouse intracerebral  $LD_{50}$  (MicLD<sub>50</sub>); this is about one million times more than required for foxes. In contrast, foxes were susceptible to low doses of a canine rabies virus from North Africa, but they resisted the injection of higher doses and became immune (Blancou *et al.*, 1983). Fekadu *et al.* (1982) inoculated dogs with Ethiopian and Mexican street rabies viruses and found significant mortality with doses as low as 1.7 MicLD<sub>50</sub>. In another study dogs were found to be highly susceptible to a jackal isolate, where 1 MicLD<sub>50</sub> caused infection (Bingham, 1999). Dogs are also susceptible to Mokola virus and to experimental Lagos bat virus infection (Percy *et al.*, 1973; Tignor *et al.*, 1973; Foggin, 1983). Dogs challenged with ABLV showed intermittent mild neurological signs but recovered fully by 90 days with sero-conversion and no evidence of residual virus; antibody in cerebrospinal fluid (CSF) in some of the dogs supported the notion that these dogs had had CNS infection with ABLV, but had cleared the infection (McColl *et al.*, 2007).

No mammal studied so far is completely refractory to rabies virus infection under experimental conditions. However, there are marked differences in susceptibility to intramuscular injection as demonstrated by Sikes (1962), Parker and Wilsnack (1966), Blancou (1988a), Steck and Wandeler (1980), and others. The outcome of an exposure is not only subject to the host in question, but also dependent on properties of the infecting virus variant (Blancou, 1988a). The basis for species differences in susceptibility and how susceptibility is linked to specific properties of virus variants is not understood, though Baer *et al*. (1990) speculated that the abundance of nicotinic acetylcholine receptors at the entry port would explain the contrast in susceptibility.

#### Incubation

The time between exposure and first appearance of clinical signs of disease may range from days to years, but the majority of incubation periods observed after experimental inoculation are between 3 and 6 weeks. Incubation periods in dogs observed after natural exposure in Zimbabwe are mostly between 2 and 5 weeks (Foggin, 1988). Hampson *et al.* (2009) found the incubation to be mainly between 20 and 25 days. Usually, greater viral input leads to a shortened course and vice versa (Fekadu *et al.*, 1982; Fekadu, 1991b), but these oftencited relationships are not entirely clear, being complicated by site of viral entry, immune status, origin of virus, and other factors.

At the entry (inoculation) site, virus replication can be detected in myocytes or in other cells. It is not altogether clear if that is an obligatory step before it gains access to the nervous system or if direct entry into peripheral nerves is the rule (Charlton, 1988, 1994). The transport of rabies virus in the form of genomic RNA, RNP or virions to the CNS in motor and/or sensory fibres is in the axons by retrograde axoplasmic flow (Tsiang et al., 1991). Combined active and passive immunization very shortly after exposure mediates the elimination of the virus before it enters the nervous system. In laboratory rodents it is possible to interrupt the transport to the CNS by amputation of the inoculated limb or by neurectomy within a short period after inoculation (Baer et al., 1968).

There is usually no measurable immune response to rabies during the incubation period. However, an antibody response can be observed when animals are injected experimentally with inocula that not only contain infectious virus, but also high amounts of non-infectious viral proteins, or with a virus variant adapted to a different species (Blancou et al., 1983; Hill and Beran, 1992). Several factors may contribute to this phenomenon: low antigenicity of the inoculum and rapid sequestration within peripheral cells and nerves, immunosuppressive effects of rabies virus (Wiktor et al., 1977), and possibly immunodepressive properties of saliva (Tsiang and Lagrange, 1980).

#### **Central Nervous System Infection**

The virus arrives in the area of the brain or spinal cord having direct neural connections with the inoculation site. In the CNS the virus replicates in the perikarya of neurons; other cell types are only sporadically infected (Iwasaki, 1991). The transmission of virus from one neuron to another is probably mostly by budding on postsynaptic or adjacent plasma membranes, followed by endocytosis on or near synaptic junctions (Charlton and Casey, 1979). There is also some virus budding into the intercellular space. Viral dissemination within the CNS is due mainly to retrograde and anterograde axonal transport. The pathology and the distribution of rabies virus antigen in the CNS are well described (Charlton, 1988; Perl and Good, 1991). Antigen distribution is quite variable. It depends on the site of inoculation and on the infecting virus variant, and may also be more visible in certain (large) cells. Lesions, as visible by standard histology, are usually relatively mild and include some perivascular cuffing, slight neuronophagia and gliosis, and moderate inflammation of meninges. The extent of inflammatory lesions appears to be proportional to the length of the morbidity period (Fekadu et al., 1982). The clinical symptoms resulting from CNS infection are certainly the expression of damaged neuronal functions. However, not all behavioural changes are easily explained by the areas of the CNS most obviously affected.

## Peripheral Organ Involvement and Excretion

There is extensive infection of peripheral organs in late stages of the disease. Virus replication in the CNS allows a centrifugal spread. Again, the virus moves passively inside axons. Rabies virus antigen can then be detected in most organs (Charlton and Casey, 1979; Balachandran and Charlton, 1993). Often it is limited to nerve fibres and ganglia. Replication in extraneuronal tissues is evident in the exocrine cells of salivary glands, lachrymal glands, and pancreas; frequently in myocytes of muscles; and occasionally in other tissues such as tonsils and cornea. The virus concentration in peripheral organs can be high, often reaching titres of more than 10<sup>6</sup> MicLD<sub>50</sub> per g of tissue (Fekadu and Shaddock, 1984; Baer and Wandeler, 1987; Fekadu, 1988, 1991b). A possible role of tonsil infection and virus excretion by asymptomatic 'carrier state' animals is discussed by Fekadu et al. (1983).

The WHO (World Health Organization) Expert Committee on Rabies recommends that clinically normal dogs and cats having bitten a person be observed for 10 days. The recommendation is based on two observations: (i) that virus excretion with saliva occasionally occurs a few days before clinical symptoms are detectable, and (ii) that antigen detection in the brain of an infected animal during incubation or in prodromal phases is not always possible. In experimentally infected dogs Vaughn et al. (1965) and Fekadu et al. (1982) observed virus excretion up to 7 days, but in one case 14 days before the onset of clinical symptoms. Some animals never excrete virus with their saliva, some may excrete intermittently. Foggin (1988) found that only 72% of rabid dogs had viable virus in the salivary glands. Histological examination revealed that some salivary glands in which no virus could be isolated had inflammatory lesions consistent with those found with rabies infection (Foggin, 1988).

#### **Clinical Symptoms**

There is no single symptom that would unfailingly identify a clinically ill animal as rabid. The clinical symptoms are highly variable (Tierkel, 1975; Baer and Wandeler, 1987; Fekadu, 1991b). During the initial period of sickness there may be increased nervousness and irritability, hyperactivity, tremor, hypersensitivity, abnormal vocalization, abnormal sexual behaviour, and dyspnoea, sometimes accompanied by elevated body temperature. These prodromal symptoms usually evolve very rapidly, within hours or a few days, into more advanced stages. Based on the manifestation of predominant paralysis or of excitability, the clinical syndrome is classified as dumb (paralytic) or furious. Animals displaying the dumb form may lie quiet for extended periods. Other frequently observed symptoms are pupillary dilatation, protrusion of the third eyelid, and partial paralysis of the lower jaw and tongue, leading to drooling of saliva. The dumb form is common in dogs. The furious form is characterized by marked irritability and restlessness; objects within reach are attacked, and if small enough often devoured (allotriophagia). However, dumb phases may alternate with furious stages in a single individual. Even animals in a dumb phase may have a tendency to bite when they are

provoked and they may snap into the air. In all species the clinical illness progresses toward extensive paralysis, with or without convulsions, and then stupor and death. The range in length of illness from the onset of symptoms to deaths is from a few hours to a week, and is rarely longer than 10 days. Numerous authors provide evidence that rabies virus infection with involvement of the CNS is not invariably fatal (Bell, 1975; Fekadu and Baer, 1980; Fekadu, 1991a). Bell *et al.* (1972) did not find any CSF antibodies in clinically healthy dogs in a survey in an enzootic area in South America, and concluded that nonfatal rabies is very uncommon.

#### **Diagnosis and Surveillance**

#### Clinical diagnosis

Often rabies is diagnosed on the basis of clinical symptoms. Rapidly worsening symptoms in a dog, as described above, and the almost invariably fatal outcome are strong indications for the presence of a rabies virus infection. There is considerable variation in the clinical course within and between species. In addition, symptoms that are considered pathognomonic may never develop. Nevertheless, Tepsumethanon et al. (2005) developed criteria that allowed them to make a correct rabies diagnosis in over 90% of suspect dogs kept under observation. According to the authors the occurrence of at least three of the following signs makes it likely a clinically suspect dog is indeed infected by rabies virus:

- drooping jaw;
- abnormal sound in barking;
- dry, drooping tongue;
- licking its own urine;
- abnormal licking of water;
- regurgitation;
- altered behaviour;
- biting and eating abnormal objects;
- aggression;
- biting with no provocation;
- running without apparent reason;
- stiffness upon running or walking;
- restlessness;
- bites during quarantine;

- appearing sleepy;
- imbalance of gait; and
- frequent demonstration of the 'dog sitting' position.

It is therefore advisable to consider as suspect rabies cases all instances of rapidly progressing neurologic disorder in the absence of binding alternate diagnosis. Distemper, infectious canine hepatitis, pseudorabies, and a number of other canine diseases causing neurological disorders may be considered differential diagnoses. Clinically suspect cases of rabies must be submitted for laboratory confirmation when they have contaminated (bitten) humans or when essential for epidemiological surveillance.

#### Laboratory diagnosis

Current laboratory tests are described in detail in the WHO publication *Laboratory Techniques in Rabies* (Meslin *et al.* 1996), in the OIE *Manual of Standards for Diagnostic Tests and Vaccines* (2008), and in numerous other publications (Webster and Casey, 1988; Sureau *et al.*, 1991; Trimarchi and Debbie, 1991).

The method of choice is immunofluorescence for the detection of viral antigen in brain impression smears. Impression smears of selected parts (which must include hippocampus, brainstem, and medulla oblongata) of the dissected brain are made on microscopic slides. The air-dried smears are fixed in acetone and then incubated with a fluorescein-labelled anti-rabies (preferably anti-RNP) immunoglobulin preparation. The smears are then washed in buffer to remove excess conjugate, and examined with UV microscope. Cytoplasmic viral antigen accumulations, mostly in the form of RNP, appear as fluorescing polymorphic inclusion bodies in perikarya and dendrites. The method is highly specific. Nevertheless, the diagnostician has to take into account that naturally occurring pigments may fluoresce, and that conjugates bind nonspecifically to a number of structures (sometimes by mediation of Fc receptors), especially to contaminating bacteria. The maintenance of proficiency of diagnosticians must be assured.

The demonstration of inclusion bodies in neurons with histological staining methods is less reliable. It gives accurate results in only about 80% of the positive cases when compared with immunofluorescence. Immunohistochemistry on paraffin or frozen sections is highly reliable. This is the method of choice if formalin-fixed tissue is the only material available (Bourgon and Charlton, 1987; Feiden *et al.*, 1988). This method is relatively slow, costly, and requires histology equipment.

The PCR test, which detects and amplifies specific nucleotide sequences, has become important as a back-up test in many modern laboratories. Nucleic acid amplified in PCR tests can be used for sequencing, which is useful for virus characterization. There are different variants of the PCR assay, and real-time PCR, using TaqMan® technology (Life Techonologies, Carlsbad, California) is particularly useful as it can be completed with hours and is less prone to contamination than more convention PCR assays. PCR tests have high analytical sensitivity for the particular virus variants for which they have been designed. However, they are liable to miss variants with minor differences in the genetic sequence to which their probes are targeted. Diagnosticians must be particularly vigilant to this possibility.

A number of other methods have been described. The ELISA test has not been widely used, probably because it offers no additional advantages over other immunological test methods. More recently a direct rapid immunohistochemical test (DRIT) has been developed at the rabies laboratory of CDC, Atlanta, Georgia. Biotinylated monoclonal antibodies are used to detect rabies nucleocapsid antigens in brain smears. The test is similar in sensitivity and specificity to the FAT (fluorescent antibody test), but has the advantage that fluorescence microscopy is not necessary. The test has therefore been recommended for situations where a sophisticated laboratory is not readily available (Lembo et al., 2006; Dürr et al., 2008). In addition, rapid immunochromatographic tests have been developed and evaluated (Kasempimolporn et al., 2011). These tests detect rabies antigen within minutes and do not require any laboratory facilities.

With all diagnostic tests, it is highly advisable that results are confirmed by one or more additional tests. Confirmatory tests are especially important when results are negative in suspicious cases with histories of human exposure. Where uncharacterized lyssavirus variants are likely to occur, and where test validation methods are limited, virus isolation procedures in either mice or cell cultures are particularly useful. Virus isolation amplifies the virus, allowing a better chance of detection; however, such tests require the use of other detection methods (immunofluorescence, PCR, or ELISA) to confirm the presence of the virus. Also, they require days or weeks to complete and are therefore not suitable for diagnosis where urgent medical decisions are needed.

#### Material suitable for surveillance

Specimens can be brought or shipped to the diagnostic centre as whole carcasses, heads, extracted whole brains, or brain samples collected through the foramen magnum or the orbita with a straw or another suitable probe. The specimens should be transported frozen or refrigerated. It is advisable to transport small pieces of brain (brain stem, medulla oblongata, hippocampus) in 50% buffered glycerol if circumstances do not permit a rapid and refrigerated delivery to the laboratory. One might also consider submitting fresh material, and in addition to fix half of each brain in formalin for histological or immunohistological processing.

Brain specimens from animals that have acted suspiciously or that have contaminated humans are the material most desirable and suitable for surveillance. Their submission to a diagnostic laboratory should be encouraged. Dogs, wild Carnivora, and bats are the species most often recognized as principal hosts. Other domestic Carnivora (cats, etc.), domestic herbivores, and wild ruminants are quite often victims of the disease, but they only rarely support epizootics independent from the before-mentioned species. Clearly not suitable for surveillance are rodents and birds, as well as clinically normal animals and roadkill. This is not to state that such material should never be examined in well-defined projects, but it is very likely that the disease prevalence among them is extremely low. It is also not recommended to base rabies surveillance on serology.

There is a host of reasons why serology can be misleading. Antibodies can be measured in neutralization tests (assayed in mice or in tissue culture). The most outstanding but rarely acknowledged problem in neutralization assays are virus-inactivating properties that occur quite frequently in blood collected under suboptimal conditions. The problems with nonspecificity that must be overcome in haemagglutination inhibition tests and ELISAs are profound. If one accepts a positive result as real, then one is left with the question of the cause. Serum antibodies are usually not of very high titre and are not accompanied by CSF antibodies if they are the result of vaccination. Antibody titres are very high in serum and in CSF if they are the corollaries of survival of clinical disease, which is considered to be exceptional. We do not know what antibody levels to result from different forms of abortive infections and noninfective natural exposures (e.g., oral). In addition, the possibility of cross-reacting rhabdovirus antibodies has never been investigated properly.

#### Obligations of the diagnostic centre

The most obvious duty of the diagnostic centre is to achieve diagnosis rapidly and to report quickly, to permit timely post-exposure prophylaxis and disease control decisions. A diagnostic centre is more useful if it serves a large area, and not only its immediate vicinity. It is a formidable task to ensure the submission of specimens from all regions that require diagnostic services and/or need surveillance. It might not be achievable without a network of motivated and well-instructed personnel in agricultural and health services in all regions concerned.

The diagnostic centre should give instructions for sample conservation, packaging, completion of submission forms, and transport. The field personnel must also be advised on the purpose of sample submissions and on what categories of specimens to collect. The diagnostic centre has to supply material for conservation and packaging if these are not readily available in the field. It also should provide blank submission forms. Submission forms should accompany every specimen. They should furnish the following information:

- species;
- date (of submission);
- location (where animal was found);
- owner's name and address (for domestic animals);
- type of human exposure (none, bite, other);
- date of exposure; and
- names and addresses of exposed people.

A number of items of supplementary information might also be collected, such as clinical symptoms, whether the animal was killed or found dead, age and sex of the animal, and observations on the source of infection.

The diagnostic centre should perform a number of additional duties aside from assisting sample submission and achieving laboratory diagnosis. A serotype/genotype identification and/or rabies virus variant characterization should be performed on some, possibly all, specimens found positive in routine testing. Selected samples should be forwarded to laboratories qualified to perform this task if it cannot be achieved in the diagnostic centre. Reference samples need to be set aside. They should be stored as original rabid brain samples, or as virus isolates made thereof, at -70°C, or better still, in liquid nitrogen or in lyophilized condition. The goals of specimen selection for long-term storage are to cover epizootic events spatially and temporally, and to represent all virus variants that might circulate independently.

Last but not least, it is the diagnostic centre's duty to analyse the findings or to make them available for analysis, and to produce monthly, quarterly, or yearly reports. None of the classical epidemiological parameters such as incidence and prevalence are very useful: the specimens submitted to the diagnostic centre do not constitute a random sample. A random sample, if one would attempt to analyse one, would have to be enormously large due to the very low prevalence of detectable rabies infections in a population (the infection is not readily detectable in its incubation stage). However, simple periodical maps and tables listing by species and area of origin the numbers examined and the numbers found rabid will indicate trends and movements.

## Rabies Surveillance and Rabies-Free Status

The objective of rabies diagnosis of an individual suspect animal is to enable post-exposure prophylaxis decisions. Disease surveillance has additional objectives, such as establishing an understanding of the epidemiology (this will allow the formulation of strategies for public health measures, which includes postexposure prophylaxis policies), and also to promote public awareness to permit diseasecontrol planning. Adequate surveillance is essential for monitoring the impact of disease control operations and for maintaining rabies-free status.

According to the WHO (2005) and the OIE International Code (OIE, 2011), the recognition of rabies-free status of a country or area is dependent on the following preconditions:

- Rabies is a notifiable disease.
- An effective system of disease surveillance is in operation.
- All regulatory measures for the prevention and control of rabies have been implemented, including effective importation procedures.
- No case of indigenously acquired rabies infection has been confirmed in humans or any animal species during the past 2 years (some exceptions may apply).

#### Epidemiology

Rabies viruses are adapted to the physiological traits and the population biology of their principal hosts (Bacon, 1985; Wandeler, 1991a; Wandeler *et al.*, 1994). They have a host-specific pathogenicity and pathogenesis. Adaptation of a particular virus variant to its principal host is indicated by the frequency and magnitude of its excretion on one hand, and by the host's high susceptibility to it on the other hand. These properties allow for transmission from an infective to a susceptible individual in the event of a biting incident. This has been documented to some extent by in vivo experiments on susceptibility, and by observations on virus excretion in experimentally infected animals and in field specimens submitted for diagnosis (Blancou, 1988a; Blancou et al., 1991). Viruses either take advantage of normal mechanisms of social interaction or they promote infectious contacts by changing host physiology and behaviour. Rabies virus, possibly by altering specific neural functions (Charlton, 1994), causes aggressiveness as a prevailing feature among induced behavioural changes. However, susceptibility, aggressiveness, and virus excretion are insufficient attributes for allowing a prolonged persistence of the virus in a host population. Encounters between infective and susceptible individuals leading to transmission must occur at the correct frequency. These and other significant aspects of viral host adaptations are more difficult to explore experimentally.

## Dog Rabies in Different Regions of the World

There are areas where we observe enzootic dog rabies, and areas where the disease in dogs must be considered as spillover from wildlife rabies. Domestic dogs have been the principal hosts of rabies in Europe, the Middle East, and Asia for thousands of years (Baer et al., 1996; Blancou, 2004; Neville, 2004). In contrast, dog rabies has been a more recent phenomenon in other parts of the world. In North America it was first reported in Mexico early in the 18th century (Baer et al., 1996). It was first recorded in South America in the beginning of the 19th century (Steele and Fernandez, 1991). In sub-Saharan Africa rabies was noted for its absence by early European explorers in the middle of the 19th century, and was first reported in dogs in several countries in the early 20th century

(Swanepoel, 2004). Probably it was only relatively recently introduced into regions where it is now endemic (Nadin-Davis and Bingham, 2004). In recent decades in large parts of Asia, Africa, and Latin America, rabies virus circulates in the dog population. Between 75% and 99% of all reported cases are in dogs (Turner, 1976; WHO, 1984; Acha and Arambulo, 1985; Blancou, 1988b). Canine rabies is occasionally coined 'urban rabies'. However, in many countries it is more a problem of periurban and densely populated rural areas, while the frequency in cities remains relatively low.

In Europe, dog rabies declined after World War I. In North America rabies was maintained principally by dogs until after World War II. In the second half of the 20th century rabies was prevalent in wild Carnivora in Europe, North America north of Mexico, and in parts of Southern Africa. In those areas only 0.1–5% of the rabies cases reported annually were in dogs (Tabel et al., 1974; Steck and Wandeler, 1980). Three factors may account for the low prevalence of rabies in dogs: (i) most dogs are restricted in their movements; (ii) they are kept indoors or in enclosures and leashed when outside; and (iii) dog vaccination is strongly recommended or even compulsory. It may also be that virus strains adapted to wild species are not very well suited for propagation within dog populations. There is no recent evidence that wildlife rabies provoked epizootics in stray dog populations in the United States or in Europe.

#### Canine Rabies

From information given by Glosser *et al.* (1970), Beran *et al.* (1972), Belcher *et al.* (1976), Mitmoonpitak *et al.* (1998), and Fekadu (1982), one gets the impression that dog rabies is highly enzootic with only moderate fluctuations in prevalence. This picture is only partially correct, since epizootic patterns have also been described, for example by Bingham *et al.* (1999), Eng *et al.* (1993), Hampson *et al.* (2009), and Waltner-Toews *et al.* (1990), and Zinsstag *et al.* (2009). Apparent prevalence can be influenced by surveillance coverage,

particularly the scale of case analysis, and for this reason, examination of whole-country data will tend to even out more local epidemic trends (Bingham, 2005).

Rabies in dogs generally does not follow a marked seasonal trend in prevalence as it does in many wildlife maintenance hosts (Blancou et al., 1991; Bingham et al., 1999), although Swanepoel (1994) does record a pronounced seasonal trend for dog rabies in the Natal Province of South Africa. Seasonality in wildlife hosts has been hypothesized to occur as a result of their highly seasonal breeding patterns and seasonal territorial instincts, both characteristics which are less well developed in dogs. Domestic dogs tend to breed throughout the year, though seasonal fluctuations of bitches in oestrus and in pregnancy can be observed in some areas (Totton et al., 2010a).

Epidemics of rabies in dogs are usually not clearly confined behind advancing geographical fronts, as has been reported for a number of wild carnivores (Bingham et al., 1999). This may be due to the poor surveillance of dog rabies in countries which do not have developed infrastructures. However, a spatially less structured epidemiology may be typical of the disease in this species. Dog rabies epidemics are probably spread to a large degree by human activities, for example in cars, buses and fishing boats (e.g. onto the islands of Flores in 1997 and Bali in 2008), as dogs incubating the disease will be moved by their owners to new homes. In addition, dogs will often accompany their owners on foot over long distances, well out of their normal home ranges, and rabid dogs sometimes move long distances on their own (Butler, 1998; Hampson et al., 2009).

Rabies in many dog populations appears to rank high as a cause of adult dog deaths. Although official statistics will often not indicate high prevalence rates of rabies, the disease is frequently found when actively searched for. For example, Beran *et al.* (1972) found that 23.6% of deaths in adult dogs in the Philippines were due to rabies. However, prevalence may vary considerably with time, particularly at local scales.

The epidemiology of rabies is generally not very well understood. Incidence, prevalence, and recovery rates are difficult to record. Unfortunately this also holds true for dog rabies in spite of the easy access to dog populations. Though thorough analyses of dog rabies epidemiology remain rare, the combination of field observations and modelling has provided some new insights for areas in sub-Saharan Africa. An important analysis was performed in N'Djaména in Chad (Zinsstag et al., 2009). The estimated transmission rates between dogs were  $0.0807 \,\mathrm{km^2/(dogs \times week)}$  and between dogs and humans  $0.0002 \,\mathrm{km^2/(dogs \times week)}$ . The effective reproductive ratio was estimated to be 1.01, indicating low-level endemic stability of rabies transmission. Excellent studies were also conducted in Tanzania (Hampson et al., 2007; 2009; Lembo et al., 2008). The investigators estimated important epidemiological parameters such as incubation periods (average 22.3 days) and the infectious periods (average 3.1 days). The mean transmission distance was 0.88km, though individual rabid dogs travelled much further. The authors also calculated the average number of secondary cases produced by an infected dog, the so-called basic reproductive number  $R_0$ for the Tanzanian outbreaks, as well as from published information from other parts of the world. The ballpark R<sub>0</sub>s are between 1.05 and 1.8. Noteworthy is the statement (Hampson et al., 2009) that the basic reproductive rate of rabies appears to be independent of dog population densities. This is in contrast to the frequent statement that high-density dog populations permit the occurrence of enzootic canine rabies, though it is well-known that the disease also persists in dog populations of low density (Foggin, 1988; Butler 1998).

The rate at which infected hosts transmit rabies to healthy animals depends on the social system of the host which promotes contact between infected and non-infected individuals. Dogs are kept and tolerated at very high numbers in most human societies. Dog population densities may reach several thousand per km<sup>2</sup> (Wandeler *et al.*, 1988, 1993). This is considerably more than any wild carnivore population ever achieves. As discussed above, although the density may not be a determining factor for the occurrence of rabies, it will have an impact on the population's social organization on one hand, and on dog-human interactions on the other hand.

Most canid species, including dogs, are highly adaptable with respect to their social systems (Macdonald and Carr, 1995) and this allows for considerable variation in the social parameters which determine transmission rates. Rabid dogs will frequently display aggression and actively seek other dogs and other animals to bite. Rabid dogs may also bite following stimuli which would not normally elicit an aggressive response. There is evidence that disoriented rabid foxes (Vulpes vulpes) wander into their neighbours' range and are attacked there by the territory owner, this conflict leading to the transmission of the infection (Artois and Aubert, 1985; Wandeler, 1991a). It is quite likely that similar behavioural mechanisms operate in dogs, provoking a healthy dog to get in conflict with a diseased one. Butler (1998), in a study carried out in rural Zimbabwe, found that 15 of 24 rabid dogs wandered from their homes, some covering considerable distances, and often returning home after their journey. These dogs approached homesteads and other dogs and provoked conflicts in the process. Six of 16 dogs for which Butler (1998) obtained detailed records were seen to bite 11 other dogs (all unvaccinated) resulting in transmission to seven of the dogs.

### **Rabies Control**

For a comprehensive review of dog rabies control and updated recommendations and guidelines see the website produced by the Global Alliance for Rabies Control<sup>1</sup> and Chapter 12 by Lembo *et al.* in this book.

### **Dog Population Management**

Rabies has a high incidence in dogs in areas where the animals are poorly supervised. Attempts to reduce numbers of poorly supervised dogs and to educate owners toward responsible ownership should therefore be attempted. For this purpose the WHO/WSPA *Guidelines for Dog Population*  Management (1990) should be consulted, but see also Larghi et al. (1988), and Chapters 11 and 13 in this book. Recommended control measures include movement restrictions, reproduction control, habitat control, and removal of straying dogs. The control of movements is intended to limit social contact and access to resources (both leading to disease transmission and uncontrolled reproduction). Reproduction control may be achieved through mating restrictions, surgical sterilization, and drugs, including antifertility vaccines (Bender et al., 2009). Animal birth control programmes can be beneficial, as documented in a number of cities in India (Totton et al., 2010b). Habitat control is meant to reduce the availability of resources (litter, food, shelter). The concept of responsible dog ownership (WHO/WSPA, 1990) as applied in industrialized western nations needs to be adapted to different contexts, taking into account economic, social, and cultural constraints. It is important to understand these constraints in order to implement the most effective methods of dog population management (see Chapter 13). Community-led initiatives stand the best chance of long-term success. Heavy-handed imposed methods, such as mass-culling campaigns, will alienate communities from the goals of rabies control, and are therefore counterproductive in the longer term. Sustainable rabies control policies should be multi-faceted, and should be implementable at the community level. Central governments should support communities in establishing mechanisms to effectively manage their dogs, including circulation of relevant information, safe and ethical mechanisms for removing unwanted dogs, sterilizing those not needed for breeding, and provision of basic health services for animals.

## Prophylactic Vaccination of Dogs and Veterinary Vaccines for Parenteral Use

Most of the rabies vaccines used today for the immunization of dogs and other domestic animals contain inactivated rabies virus and dead antigen. Modern inactivated tissue culture vaccines combine safety with high immunogenicity (Chappuis and Tixier, 1982; Bunn, 1988; 1991; Precausta and Soulebot, 1991) and are efficacious in the field (Chomel et al., 1987, 1988; Aubert, 1993; Carlos et al., 1997). Cell lines and primary cell cultures are used as substrates for a number of virus strains. Several manufacturers include a variety of different antigens (distemper, adenovirus, leptospirosis, parainfluenza, parvovirus) in combined vaccines. No indications of competitive inhibition have been noted, but every new product should be investigated for its overall immunogenic potency. Inactivated nerve tissue vaccines may be prepared from the brains of lambs or suckling mice inoculated newborn intracerebrally (with fixed viruses). They may be adjuvanted. These vaccines do not always have an efficacy comparable to the efficacy of inactivated tissue culture vaccines. The use of modified live (attenuated) vaccines is no longer recommended for dog immunization, except for special situations (e.g. national campaigns under economic constraints). Live attenuated virus vaccines, such as LEP (low egg passage), HEP (high egg passage), and ERA (Evelyn Rokitniki Abelseth) have been significant components of rabies control in the past, but are no longer recommended for use in domestic animals because of problems of residual pathogenicity and/ or poor efficacy. Recombinant vaccines and other products of genetic engineering will probably become available soon

Rabies vaccines for dogs should satisfy efficacy and safety requirements as they are described by WHO (2005), OIE (2008), and by national regulatory agencies. It is recommended that vaccines are completely innocuous, even for very young animals, and that they confer immunity for 1, and preferably 2 years after one injection, in all dogs above an age of 3 months.

(Chappuis, 1997).

There are no treatment schedules or vaccines licensed for post-exposure treatment of dogs. Though this is certainly a pragmatic recommendation, the topic may require some more research. Recently, postexposure vaccination of dogs and cats has been recommended following contact with bats infected with ABLV (Animal Health Australia, 2009).

## Dog Vaccination in Areas with Wildlife Rabies

In industrialized nations with predominant wildlife rabies, dog vaccination is recommended or compulsory. Owners have to register (or license) dogs. Registration can be made dependent on the production of a certificate that the animal has been vaccinated against rabies when over 3 months old and had been revaccinated at periods of not more than 1 or 2 years. Vaccinations should be done by parenteral inoculation of a product recognized by the national authorities, usually an inactivated vaccine conferring 2 years of immunity after one injection.

## Rabies Control in Areas with Canine Rabies

Successful attempts at the control of rabies have generally occurred where both vaccination and dog control (destruction, confinement, breeding restrictions) have been practised simultaneously (Tierkel et al., 1950; Fredrickson et al., 1953; Wells, 1954). Eng et al. (1993) speculate that the outbreak in Hermosillo, Mexico, may have been linked to an increase in population density and a drop in vaccination coverage. Rabies control in areas with canine rabies is usually not a simple application of regulations on dog ownership. Their enforcement is impeded by a number of ecological and cultural constraints. But well-planned and well-executed campaigns may reduce rabies incidence in dogs drastically, and may even eliminate the disease in areas where it is not maintained by wildlife. Taking the cost and benefits of a campaign into consideration, we suggest that disease eradication should be the goal, rather than a temporary reduction of the incidence

rate. Comprehensive national, rather than temporary, local plans are imperative. These plans have to identify a goal, and they have to consider national structures and resources. Effective cooperation among all involved ministries and national and local agencies is necessary. WHO provides useful guidelines for programme management (WHO, 1984, 2005, 2009; WHO/FAO, 1990). These documents give detailed guidance on the planning and management of control programmes, on legislation, and on techniques in local programme execution.

For planning a comprehensive control programme it is necessary to consider a number of dog population parameters (size, turnover, accessibility). Vaccination coverage of about 75% of the total population should be attempted. This goal should be achieved in a particular area within a relatively short time period (a few weeks). Pilot projects may help in assessing: (i) dog accessibility, (ii) ways of cooperating with local residents, and (iii) avenues to provide information and education. Plans for large-scale operations, vaccination strategies, and logistic aspects can then be adjusted according to findings in the pilot phase. An effective maintenance programme must be part of the plan. Operational research for monitoring campaign efficiency is strongly recommended.

A number of different approaches can be taken:

1. Dog owners may take their pets to private or state veterinarians for vaccination. This is the most important way in which population immunity is achieved in the more affluent parts of the world, whereas it only accounts for a small proportion of vaccinations in less wealthy countries where there are few veterinarians within communities, or where the cost of a veterinary consultation is too expensive for many people.

2. The state veterinary services may conduct campaigns of which the most common is the central point campaign where owners are required to bring their pets to a designated place at a particular time. Such campaigns require a considerable amount of prior advertising using loud-hailers, posters, and informal local news networks. Because of this, and also because dog owners often have other priorities, or they may not be able to take all their dogs to the central point, this method usually does not reach more than 10-40% of dogs (Brooks, 1990; Beran, 1982), but can be much better if properly implemented (Wandeler *et al.*, 1993; De Balogh *et al.*, 1993).

**3.** The state vaccination teams may run a house-to-house vaccination campaign, where they visit each household and vaccinate every dog they are able to catch. The latter method, although very demanding of resources, is usually successful in achieving the 70% coverage (Korns and Zeissig, 1948; Beran, 1991; Coleman and Dye, 1996) thought to be necessary to eradicate dog rabies. In many African and Asian countries it is not used extensively due to resource constraints.

## Oral Vaccination of Dogs Against Rabies

Oral vaccination of wildlife has been applied for rabies control since 1978 (Steck *et al.*, 1982; Wandeler, 1991b). A number of live attenuated and genetically engineered vaccines have been tested for safety and efficacy in a variety of species, including dogs (Chappuis *et al.*, 1994; Fekadu *et al.*, 1996; Rupprecht *et al.*, 1998). Field trials, using live attenuated vaccines and a vaccinia rabies glycoprotein recombinant, have been assessed (Bishop *et al.*, 1999; Estrada *et al.*, 2001; Aylan and Vos, 2000; Cliquet *et al.*, 2007). However, at present there are no vaccines licensed for oral immunization of dogs.

The high number of human casualties caused by dog-transmitted rabies clearly indicates that dog rabies control either is not applied or is failing. There may be many reasons for not reaching a sufficient level of herd immunity in dog populations by parenteral vaccination, including inadequate logistics, insufficient community participation, and large numbers of ownerless dogs. It is often thought that a majority of these problems could be solved with an oral vaccine for dogs. This notion can only be partially correct. Baits broadcasted over a landscape, as done for wildlife immunization, will reach various segments of a dog population very differentially, though other distribution models may be applied (Frontini et al., 1992; Matter, 1997; Ben Youssef et al., 1998). One has to visualize that dog population densities can reach several thousand individuals per km<sup>2</sup>: this is between 100- and 1000-fold the densities of wildlife populations targeted for rabies control by oral immunization. Logistics will not be simpler than with parenteral vaccination campaigns. The number of vaccine doses that do not reach the target (immunize a dog) is higher than with parenteral vaccination. The likelihood of human exposure to vaccine is much higher than in wildlife vaccination campaigns. It is therefore essential that oral rabies vaccines for dogs meet higher safety standards than those presently applied to wildlife immunization. However, compared to parenteral inoculation, a vaccine that can be administered orally will reduce distress in the vaccinator, the animal owner, and the animal to be vaccinated. This permits the immunization of dogs that otherwise cannot be handled, and facilitates community participation if properly advertised. In view of these advantages WHO supports the concept, and convened a number of consultations to outline efficacy, safety for target and non-target species including humans, and logistic aspects (WHO, 1989, 1990, 1992b, 1993, 1994, 1995, 1998, 2007). The WHO consultations recommend that only 'door to door' and 'hand out' techniques, with recuperation of baits and bait fragment if not taken, are considered for initial field trials.

#### **Maintenance of Rabies-Free Status**

The WHO Expert Committee on Rabies recommends that countries free from rabies should prohibit the importation of certain species of mammals and/or permit their entry only under the authority of a licence granted previously. Earlier WHO Expert Committee reports state that 'on entry, such animals should be subjected to a prolonged period of quarantine, preferably 4 months or more, on premises approved by the Government veterinary service' (7th report, 1984). Only in its 8th report (WHO, 1992a) was the Committee discussing a system of animal identification, vaccination, and serology as an alternative, where strict quarantine measures are impractical. In its 8th report the Committee recommended taking into account a number of considerations when contemplating import regulations:

- incubation periods are variable, from a few weeks to more than 6 months; very long incubation periods are rare;
- the immune response to vaccine in immature animals is inadequately defined; it is certain that circulating neutralizing antibodies persist for shorter time periods than in adult individuals;
- immune responses also vary with vaccine type, immunization procedure, condition of animal (e.g. parasite load) etc.;
- animals vaccinated during incubation may develop antibody, but disease may not be prevented;
- false-positive results occur in current serological tests;
- misidentification of animals, certificates, and serum samples occur; and
- the impact of rabies-related viruses and variants of low pathogenicity for dogs is unknown.

The 1st report of the WHO Expert Consultation on Rabies (WHO, 2005) gives more detailed recommendations, and so does Chapter 8.10 of the OIE Terrestrial Animal Health Code (OIE, 2011).

## The Prevention of Human Rabies

Important components of the prevention of human rabies are the avoidance of potentially infectious contacts, and the proper prophylaxis after exposure. Both should be advocated by public health education. Such education should include information on the epidemiology, clinical signs in animals, zoonosis control, and wound treatment after exposure, and should indicate that proper immunotherapy should begin as quickly as possible. Pre-exposure prophylactic immunization is recommended only for people with an elevated exposure risk, such as veterinarians and laboratory personnel. Post-exposure prophylaxis (PEP) should follow national guidelines, which are usually based on WHO recommendations (WHO, 2005, 2010a). Immediate and thorough cleansing of bite wounds is an important first step. The circumstances and nature of the suspected exposure should be considered in all decisions for further treatment. PEP should be given when a bite by a suspicious animal or a contamination of mucosa or broken skin with potentially infectious material has occurred. Combined active immunization with vaccine and passive immunization with rabies immune globulin is considered the best post-exposure prophylaxis.

Rabies in dogs is a significant threat to human health. Worldwide, an estimated 30,000-60,000 people die of rabies every year (Knobel et al., 2005). The number of people receiving post-exposure treatment - mostly after dog bites - was judged to be about 3.5 million per year (Bögel and Motschwiller, 1986; Bögel and Meslin, 1990), while a WHO document (WHO, 2010b) puts this figure at 14 million post-exposure treatment applications each year. China and India alone account for almost 90% of the word consumption of rabies vaccines. Almost all human rabies deaths, and the vast majority of treatments after bite exposures, occur in developing countries (Acha and Arambulo, 1985), in areas where dog rabies is prevalent (Baer and Wandeler, 1987). This may in part be due to a high rate of exposure to biting dogs (Eng et al., 1993). The highest figures come from South and South-East Asia, where the annual exposure to dog bites is between 2% and 5% of the population (Sudarshan et al., 2007; Xu et al., 2010). Not all biting dogs are infected with rabies, and not all bites by rabid dogs lead to clinical rabies in the bite victim. Still, up to four human rabies deaths per 100,000 inhabitants are recorded in some areas (Wandeler *et al.*, 1988, 1993).

The widespread occurrence of human rabies is due not only to the frequency of exposures, but also to the failure of applying proper treatment after bites from rabid animals. The appropriate treatment may not be available (spatially, temporally, socially, economically), or it may not be in compliance with traditional (religious) beliefs. It is also possible that the necessity of the appropriate treatment is not recognized because other treatments are considered equivalent or superior, or because the disease entity is not recognized. An inquiry into rabies deaths in Sri Lanka revealed that a good proportion of dog-bite victims resort to traditional dog-bite specialists. Some, but not all, victims also seek post-exposure immunoprophylaxis. The success rate of the traditional healer may appear to the casual observer as respectable, in view of the low frequency of rabies transmission by mostly healthy biting dogs (Wandeler *et al.*, 1993).

## Questions, Research Needs, Operational Research

A few significant studies have provided new insights into the epidemiology of dog rabies (Hampson et al., 2007, 2009; Lembo et al., 2008). Most of these were conducted in East Africa; similar investigations are largely absent in other areas with dog rabies problems. It is rather awkward that more thorough studies on dog rabies epidemiology are so rare. Structural constraints and a shortage of resources may often preclude a suitable epidemiological surveillance and data analysis. On the other hand, the easy access to dog populations should allow collection of valuable data. A systematic collection of detailed case histories could identify possible sources of infection, incubation periods, vaccination records, and contacts with other animals and humans. That this can lead to spectacular new insights has been adequately documented by the Tanzanian studies.

A number of dog populations in different parts of the world and in different ecological and cultural settings have been studied in recent years. Dog population biology is reasonably well explored. Nevertheless, one has to remember that tolerance, supervision, availability (accessibility) of resources, and other aspects of the 'habitat carrying capacity' are human cultural traits that vary dramatically from area to area. Attributes of culture not only determine dog population characteristics, but also their accessibility for control operations. Questionnaire surveys produce information on such features as dog:human ratios, dog-keeping practices, reproduction, and morbidity and mortality. Such data relate only to the owned segment of a dog population, taking into account that the ownership status of a dog may change, according to criteria applied. If there is a suspicion that a substantial proportion of dogs escape recording, one should resort to an experimental approach, as used by wildlife biologists. Modified mark-recapture techniques can be implemented without too many difficulties during mass vaccination campaigns. Such 'operational research' conducted in conjunction with pilot projects may provide a large amount of useful data. Pilot projects in general may help in assessing (i) dog accessibility, (ii) ways of cooperating with local residents, and (iii) avenues to provide information and education. Plans for large-scale operations, vaccination strategies, and logistic aspects can then be adjusted according to findings in the pilot phase. We also suggest that in future programmes, some operational research be conducted in order to monitor campaign efficiency.

Human–dog relations are significant factors in dog rabies epidemiology and control. Studies on this topic in non-industrialized nations (such as Luomala, 1960; Frank, 1965; Meggitt, 1965; Latocha, 1982; Savishinsky, 1994) are usually ignored, while the affinity of people to their pets in industrialized societies has received considerable attention by human–animal-bond champions (see Chapter 1 by Beck and Chapter 2 by Turner *et al.*). Dog ownership can have very different meanings in different cultures and is not always easy to define in Western legalistic terms. The tolerance granted to dogs must find explanation in processes of socialization and psychology. Cultural conventions determine the level of supervision of their social interactions and access to resources (food, water, shelter, mates), which is partially a function of the density and structure of human settlements. Education towards responsible dog ownership and disease prevention must conform to cultural conditions.

The ultimate purpose of rabies control is the protection of humans from both infection and economic loss. It is obvious that the elimination of dog rabies, and also the prevention of human rabies, has not made the progress one once expected (Bögel et al., 1982). In view of the high efficacy of modern post-exposure prophylaxis, nearly all human rabies cases must be considered as failures of the medical system; the correct treatment was not applied, or not applied in time. We will have to pay more attention to the ethnomedical aspects of human rabies. More inquiries into health systems and the ethnology and sociology of preventing and curing dog-transmitted diseases are clearly indicated. With this knowledge it becomes possible to implement effective and meaningful health education on how to deal with dogs, how to avoid exposure, and what to do if an exposure occurs.

#### Note

<sup>1</sup> www.rabiesblueprint.com, accessed 7 June 2012.

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# **5** Dogs and Bacterial Zoonoses

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The pleasures of dog ownership are certainly evidenced by the popularity of pet dogs in the human population. Such a relationship with dogs started with their domestication in Mesolithic times. This brought many advantages, but also placed human beings at a greater risk for exposure to dog parasites and pathogens. Dog is still the main reservoir and vector of rabies to humans worldwide (Wunner and Briggs, 2010). The discovery of parvovirus infection in dogs in the late 1970s has raised concern over the role of dogs in the transmission of that agent to humans, as well as the potential role of dogs in the transmission of rotavirus and coronavirus. Several parasitic, mycotic, and infectious agents can be transmitted from animals to human beings, and are called zoonoses. There are more than 250 zoonoses, involving a variety of causative agents and mammalian animal species as definitive or intermediate hosts. A limited number of these are caused by bacterial agents and have dogs as the main host species. However, these have a significant public health impact as some of them, though mild, are widespread; while others can be severe or even fatal. Prevalence of zoonoses transmitted from dogs to humans is rather difficult to estimate and will depend on numerous factors: number of infected animals, mode of

transmission of the agent, behavioural characteristics of the owners, and existing measures of prevention. Usually, children are at greater risk than adults, because of their closer physical contact with household dogs and their own behaviour, including putting objects in their mouth or eating non-food items, and exploration of the environment. The emerging trend of bed sharing with pets, including dogs, is also of concern in terms of potential zoonotic contamination in many developed countries (Chomel and Sun, 2011). The present chapter will focus on the bacterial zoonoses associated with dogs. A review of current concepts of bacterial dog-associated human diseases is useful, to provide objective information to the dog owner on pet care and management.

## **Bite-Associated Bacterial Zoonoses**

Animal bites represent about 1% of all emergency department visits. Between 70% and 90% of these visits are caused by dog bites (Tan, 1997). In 2001, more than 350,000 people were treated in US hospital emergency departments for non-fatal dog-bite-related injuries (CDC, 2003). Children are more likely to be bitten than adults, and males are twice as likely to be bitten by dogs as females. It is

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estimated that only 3-5% of dog bites will become infected. Most infections associated with dog bites are polymicrobial, with Staphylococcus spp., Streptococcus spp., and Corynebacterium spp. as the most frequently isolated aerobic organisms (Griego et al., 1995; Talan et al., 1999). Additionally, anaerobic bacteria, including Bacteroides and Prevotella spp., are present in 38-76% of dog bite wounds (Brook, 1987; Alexander et al., 1997). Porphyromonas spp. have been isolated from 28% (31 of 110) of specimens from infected dog and cat bite wounds of humans (Citron et al., 1996). Human cases of infection after dog bites also include septicaemia caused by commensal bacteria of the oral flora of dogs, such as Weeksella zoohelcum, Neisseria weaveri (Canton et al., 1987). However, bite-related zoonotic bacteria mainly include Pasteurella spp. and Capnocytophaga canimorsus. A new bacterium (NO-1) has recently been associated with dog and cat bites.

## Pasteurellosis

Pasteurellosis is commonly associated with dog bites and even more frequently with cat bites. Pasteurella spp. are commensal bacteria of the oral cavity of dogs and cats. The subtypes associated with human infections include P. multocida subsp. multocida, P. canis, P. multocida subsp. septica, P. stomatis, and P. dagmatis (Oehler et al., 2009). Carriage rates of Pasteurella spp. in dogs range from 22% to 81%, but Ganière et al. (1993) indicated that pathogenic strains were found in 28% of the dogs tested (versus 77% of the cats). P. canis is the most common isolate from dog bites and P. multocida subsp. multocida and P. septica were the most common isolates from cat bites (Talan et al., 1999). Swelling, inflammation, and intense pain at the bite site a few hours after the exposure are the typical symptoms of Pasteurella spp. infection. Penicillin is the antibiotic of choice for treatment, but most patients are more frequently treated with a combination of a P-lactam antibiotic and a P-lactamase inhibitor (Talan et al, 1999). Usually, dog bite treatment includes the administration of amoxicillin-clavulanate (250 mg orally three times a day). Other options include use of second-generation and third-generation cephalosporins (e.g. cefuroxime, cefpodoxime), and doxycycline or fluoroquinolones in penicillin-allergic patients (Oehler *et al.*, 2009). Untreated infection can lead to severe complications, including abscess formation, septic arthritis, osteomyelitis, endocarditis, pneumonia, or meningitis (Griego *et al.*, 1995).

#### Capnocytophaga canimorsus infection

Capnocytophaga canimorsus (formerly DF-2), a thin, Gram-negative rod, is reported as part of the normal oral flora of 16% of dogs (Underman, 1987). Most (91%) of the known C. canimorsus bite-related human cases resulted from a dog bite (Lion et al., 1996). After the first report in 1976, at least 160 more cases have been published, including gangrene, sepsis, meningitis, and endocarditis, and a lethality rate of 30% (Oehler et al., 2009). Because of low virulence, C. canimorsus systemic infections occur more often in immunosuppressed or immuno-impaired individuals, such as splenectomized individuals (33%), alcohol abusers (24%), or persons following an immunosuppressive treatment (5%). Most cases have also been reported in persons 50 years old or more. Therefore, when fever occurs in immunosuppressed patients after a dog bite, C. canimorsus infection should be considered. Talan et al. (1999) recovered Capnocytophaga spp. from 4.7% of the dog and cat bite wounds they cultured. Onset of clinical signs of C. canimorsus infection is variable ranging from 1 day to several weeks (Krol-van Straaten et al., 1990). The condition of the initial wound at time of diagnosis may range from gangrenous to complete healing. Almost all patients present with severe sepsis and fever. Additional symptoms include shock, disseminated intravascular coagulation, meningitis, endocarditis, macular or maculo-papular rash, pneumonia, and peripheral cyanosis. C. canimorsus is susceptible to most antibiotics, and penicillin G is recommended as the drug of choice (Lion et al., 1996). The use of amoxicillin/clavulanic acid is a good alternative.

### CDC NO-1

Between 1974 and 1998, 22 bite wound isolates submitted to CDC have been designated non-oxidizer group 1 (NO-1). They are fastidious non-oxidative Gram negative rods. Of the 22 bite victims, half of them were males, but they were much younger (median age: 18.3 years) than the female cases (median age: 39 years). Fifteen (68%) of the strains were isolated from dog and 4 (18%) from cat bites (Kaiser et al., 2002). Infections in which NO-1 bacteria were isolated appear to be local (i.e. abscess and cellulitis). Following receipt of a bite wound, NO-1 infections, without severe disease, can occur in healthy persons with no underlying illness. The most common clinical features associated with NO-1 infections included purulent drainage, increased pain with erythaema and swelling, and cellulitis.

## Other bacterial zoonoses accidentally transmitted by dog bites

Other bacterial diseases can accidentally be transmitted by dog bites, such as brucellosis (*Brucella suis*), tularaemia (a few cases have been associated with dog or coyote bites), *Erysipelothrix insidiosa* infection (Abedini and Lester, 1997), and leptospirosis. Emergence of methicillin-resistant strains of *Staphylococcus aureus* (MRSA) potentially transmitted through dog bites is also of concern (Oehler *et al.*, 2009).

## Cat scratch disease and other Bartonella infections

Reports of human cases of cat scratch disease (CSD) following dog contact have been made. According to Margileth (1993), 95% of his patients had a cat-contact history and 4% a dog-contact history. However, Carithers (1985) reported in a large series (1200 cases) that 99.1% of them had a history of cat contact and was not supportive for any other animal source. A few cases of CSD have been associated with dog bites. A report from Japan of a possible case of CSD caused by a dog contact suggests that dogs could also play a role in human Bartonella henselae infection (Tsukahara et al., 1998). More recently, B. vinsonii antibodies were detected in a young girl bitten on the cheek by a German Shepherd and this Bartonella sp. should be added to the list of pathogens capable of causing lymphadenopathies in humans after a dog bite (Rolain et al., 2009). It has been recently demonstrated that these bacteria could be detected in dogs' saliva, suggesting that potentially viable Bartonella organisms may be transmitted to humans after a dog bite (Duncan et al., 2007). Several human cases of Bartonella infection with species usually found in canids including dogs (B. vinsoni subsp. berkhoffii) have been recently reported (Breitschwerdt et al., 2007, 2010; Oliveira et al., 2010).

#### **Gastrointestinal Zoonoses**

### Campylobacteriosis

*Campylobacter jejuni*, a Gram-negative enteric organism, is a leading cause of human enteritis. Food animals, especially poultry, are the major reservoirs of the organisms, and human infection usually occurs following consumption of contaminated, untreated surface water; unpasteurized milk; or undercooked meat. Campylobacteriosis has a higher incidence in AIDS patients than in the general population, causing severe, often bloody, diarrhoea and cramping, nausea, and fever (Glaser et al., 1994). Most Campylobacter infections in dog and man are caused by C. jejuni, though C. coli infection does occur. C. upsaliensis has also been reported to cause gastroenteritis in humans. Evidence indicates that contact with infected dogs, especially diarrhoeic dogs, can increase the risk of acquiring C. jejuni (Blaser et al., 1978; Salfield and Pugh, 1987). Prevalence rates range from 10-30% in healthy dogs to 50-75% in diarrhoeic dogs and puppies for C. jejuni and C. coli. In a cross-sectional study in Denmark (Hald and Madsen, 1997), 29% (21) of the 72 healthy puppies (11–17 weeks old) and 5% (2) of 42 healthy kittens tested were infected with Campylobacter (dogs: C. jejuni 76%, C. upsaliensis 19%, and C. coli 5%). Puppies are

more likely to acquire the infection and show clinical signs (watery diarrhoea lasting 3-7 days). Infection can also occur after contact with healthy dogs which are intermittently shedding the organism. It is estimated that approximately 6% of enteric campylobacteriosis is transmitted from pet animals (Saeed et al., 1993). In a more recent study of dogs attending veterinary clinics in the United Kingdom, the prevalence of Campylobacter spp. was 38% with C. upsaliensis accounting for 94 (98%) of the isolates, and C. jejuni for the remainder. Younger dogs were more likely to carry C. upsaliensis and the high prevalence of this pathogen supports the hypothesis that dogs, particularly younger animals, may be an important source of C. upsaliensis infection for humans. However the prevalence of *C. jejuni*, the most common *Campylobacter* sp. associated with disease in humans, was low (1.2%) (Parsons et al., 2010).

In dogs, symptomatic puppies usually show a 3- to 7-day course of diarrhoea with or without anorexia, fever, and vomiting (Willard et al., 1987). The diarrhoea may be watery, mucoid, or bloody. Infected dogs may not show clinical signs of disease. Risk factors associated with non-clinical shedding include high-density housing, age, and autumn seasonality. Faecal shedding of C. jejuni in the dog is age dependent and peaks in the 1st year of life. In humans, the clinical picture of Campylobacter infection is an acute onset of fever, headache, abdominal pain, and severe watery to bloody diarrhoea usually lasting less than 1 week. Rare cases of relapse, colitis, arthritis, and septicaemia have been reported.

Diagnosis of infection is based on culture of faecal material on specific media for *Campylobacter* isolation, and identification of the isolate. Control and prevention of zoonotic infection depends on interrupting contact with contaminated materials. Infected animals should be isolated from other animals and from children. Hands should be washed after handling the pet, pet's toys, and feeding utensils, and premises should be disinfected (bleach, quaternary ammonium compounds). Symptomatic treatment (fluid and electrolyte therapy) is recommended for most patients, antimicrobial therapy being reserved for severely ill individuals. Most strains of *Campylobacter* are susceptible to macrolides and fluoroquinolones (Tan, 1997), and erythromycin remains the treatment of choice for *C. jejuni* infections.

#### Salmonellosis

Salmonella spp. are ubiquitous Gram-negative bacilli which are capable of colonizing the gastrointestinal tracts of humans, dogs, and many other species of mammals, but also birds and reptiles. Salmonellosis is one of the best-known gastrointestinal zoonoses (Willard et al., 1987). Salmonella are shed in the faeces, thus the most common mode of transmission amongst animals or between animal and human is the faecal-oral route. Salmonellosis is an extremely important zoonosis with broad economic and public health ramifications. Typically, millions of cases occur worldwide every year. It has been estimated that 1% of the 40,000 annually reported salmonellosis cases in the United States are associated with companion animals (Stehr-Green and Schantz, 1987). The true incidence of salmonellosis in dogs is unknown, as it is not a reportable disease and most infections are subclinical. Furthermore, faecal samples of dogs with clinical signs of diarrhoea and vomiting are not commonly submitted for culture (McDonough and Simpson, 1996). From 1% to 30% of the faecal samples or rectal swabs taken from healthy domestic pet dogs, 16.7% of dogs boarded in kennels, and 21.5% of hospitalized dogs were found to be positive on bacteriological culture for Salmonella (McDonough and Simpson, 1996). Young dogs (< 6 months of age) may have higher prevalences than older dogs, and dogs may shed more than one serotype in their faeces (Willard et al., 1987). However, transmission of Salmonella species from dogs to humans is rare (Tan, 1997). In Canada and the United States, outbreaks of human salmonellosis related to exposure to animal-derived pet treats have been reported, involving pig ear treats, beef steak patty dog treats, and pet treats of seafood origin (Behravesh et al., 2010; Finley et al., 2008). Case-households were significantly more likely than control households to report dog contact and to have recently purchased specific brands of dry pet food (Behravesh *et al.*, 2010). Illness among infant cases was significantly associated with feeding pets in the kitchen.

Most adult dogs shedding Salmonella in their stool are asymptomatic. Salmonellosis causes clinical signs mainly in young puppies, pregnant animals, or ageing dogs. Main clinical signs, after an incubation of 3-5 days, include diarrhoea, fever, vomiting, malaise, anorexia, dehydration, and possible vaginal discharge, especially following abortion in bitches. The acute phase lasts 4–10 days. Mortality is usually low (< 10%). Recovering dogs may have intermittent diarrhoea for up to 3-4 weeks and can shed Salmonella in the stools for up to 6 weeks (Willard et al., 1987; McDonough and Simpson, 1996). In humans, gastroenteritis with fever, vomiting, abdominal pain, and watery to mucoid diarrhoea occurs within a few hours to 2-3 days after exposure to infection.

Diagnosis of the infection in dogs, based on culture of faeces or rectal swab, often follows identification of human cases in the pet owner's family. Confirmed salmonellosis or undiagnosed gastroenteritis in a family member without a known focus of exposure should prompt a testing of the house pet, even if the dog appears healthy. Young children are more likely to be at risk of developing salmonellosis from either close contact with pets or failure to properly wash their hands after handling animals. Strict hygiene and antibiotherapy, when necessary, should be recommended. Treatment is usually supportive rather than antimicrobial, as antibiotics have been shown capable of extending the period of shedding, and triggering systemic disease (Willard et al., 1987).

### Yersiniosis

Because of their close contact with humans, pets have been suspected as possible reservoirs for human infection with *Yersinia* species. Such suspicions were based on the isolation of the human-pathogenic serotypes 0:3 and 0:9 from dogs and cats on several occasions. Although *Yersinia enterocolitica* has been

isolated from dogs, sometimes up to 30%, with serotype 0:3 accounting for 17% of the Y. enterocolitica isolates (Fantasia et al., 1993), data on clinical manifestations have been very limited and the pathogenicity of Y. enterocolitica in dogs is still uncertain (Hurvell, 1981; Kapperud, 1994). In an experimental infection of dogs with Y. enterocolitica biotype 4, seroptype 0:3, dogs shed the organism for up to 23 days, and it was readily transmitted between dogs, despite the absence of any clinical sign (Fenwick et al., 1994). Limited reports of diarrhoea or bloody, mucoid stools in dogs caused by Y. enterocolitica have been published (Willard et al., 1987). Only a few outbreaks have been documented where the likely source of human infection may have been the family's pet dog. An outbreak of Y. enterocolitica enteritis involved 16 of 21 persons in four related and neighbouring families in North Carolina, United States (Gutman et al., 1973). The illness, which led to two appendectomies and two deaths, was characterized by fever (87%), diarrhoea (69%), severe abdominal pain (62%), vomiting (56%), pharyngitis (31%), headache (18%), and leucocytosis. The source of infection was suggested to have been a bitch and its litter of sick puppies. The sequential onset of disease indicated that, once it had been introduced into the households, person-to-person transmission had occurred (Gutman et al., 1973). Another case, also in the United States, involved a 4-month-old child and puppies born a few weeks prior to the child's illness. The same serotype 0:20 was isolated from the child and three puppies. Similarly, a child was reported to have been possibly infected from an asymptomatic dog in France (Hurvell, 1981).

In humans, infection may be asymptomatic. In clinical cases, after an incubation of 4–10 days, acute gastro-enterocolitis presents with fever, mucoid diarrhoea, and abdominal pain, especially in children. Extra-intestinal manifestations include cutaneous lesions, arthritis, and possibly septicaemia. Diagnosis in humans and animals is mainly based on culture of faecal materials, and identification of the serotype should be performed when a pet origin is suspected. Serodiagnosis is helpful in humans, but of limited value in dogs. Prevention of infection is based on standard hygienic measures, such as quick removal of faeces, washing of hands and fomites, and use of disinfectants (Willard *et al.*, 1987). Antibiotics of choice for treatment of *Y. enterocolitica* are aminoglycosides and trimethoprim-sulfamethoxasole.

#### Helicobacter infections

The bacterial genus Helicobacter contains at least 18 species. These organisms colonize the gastrointestinal tracts of several mammalian and avian hosts (Foley et al., 1999). Some helicobacters, such as H. canis, H. pullorum, H. heilmannii, and H. cinaedi may be zoonotic. The original description of *H. canis* was from the faeces of healthy and diarrhoeic dogs, and a child with enteritis. Helicobacter species have been involved in human peptic ulcer and neoplasia, enteritis, and inflammatory bowel disease. Household pets could serve as a reservoir for the transmission of Helicobacter spp. to humans (Stolte et al., 1994; McDonough and Simpson, 1996). Thomson et al. (1994) reported the transmission from a pet dog to a 12-year-old girl of Gastrospirillum hominis (now H. heilmannii) which caused gastric disease in both that was eradicable with treatment. A case of a 12-year-old boy presenting with chronic gastritis caused by H. heilmannii was associated to his two pet dogs, as endoscopic examination revealed H. heilmannii-like infection on biopsy samples from these dogs with sequences identical in the boy, suggesting that the boy was infected by his pet dogs (Duquenoy and Le Luyer, 2009). Chronic vomiting and subclinical gastritis are the main manifestations of dog infection with Helicobacter (McDonough and Simpson, 1996).

#### Zoonoses of the Respiratory Tract

#### Bordetella bronchiseptica infection

*Bordetella bronchiseptica* infections have been reported in several instances in humans (reviewed by Ford, 1995), causing mainly pneumonia and upper respiratory tract infections in immunocompromised individuals (Ford, 1995; Woodard et al., 1995; Dworkin et al., 1999). More than 70 cases of human infection due to *B. bronchiseptica* have been reported (Redelman-Sidi et al., 2011). B bronchiseptica is a Gram-negative coccobacillus commonly isolated from the respiratory tract of various mammals. Dogs may be healthy carriers of a small number of B. bronchiseptica in their pharynx. It was first described in 1910 as a respiratory tract pathogen in dogs (Ferry, 1910). It is one of the infectious agents involved in the highly contagious Kennel Cough syndrome. In the few human cases, pneumonia with interstitial infiltrate is the main clinical feature (Ford, 1995). Treatment with ceftazidine and ciprofloxacin cleared all respiratory symptoms in one case (Decker et al., 1991). Immunocompromised persons and their dogs should restrict their attendance at any dog gathering, such as dog shows and boarding kennels (Angulo et al., 1994). Vaccination of the dogs may help reduce such a risk, but will not eliminate it, as these dogs can still be potential carriers of the bacterium. However, vaccination of dogs with live attenuated strains may be a source of human infection. Gisel et al. (2010) reported a cultureproven case of B. bronchiseptica pneumonia in an immunocompromised host residing in a household with her dogs who had recently received live-attenuated, intranasal B. bronchiseptica vaccinations.

## Mycobacterium tuberculosis, M. bovis, and other mycobacterial infections

Tuberculosis (TB) caused by *Mycobacterium tuberculosis* is certainly a rare disease in dogs, most often resulting from a human source (Erwin *et al.*, 2004). However, the infected dog can become the source of other human infections. The increase in human cases of tuberculosis worldwide, in association with the spread of the AIDS epidemic, is of major public health concern. There is potential for infection of pet dogs, especially those owned by homeless or economically impaired persons. Because canine tuberculosis often is the marker of the disease in humans, its early recognition in dogs is essential (Clercx et al., 1992). A few cases of human-to-dog infection were recently described in the United States (Erwin et al., 2004; Hakendahl et al., 2004). Dogs get infected by infectious aerosols from the tuberculous owner or by sniffing infectious sputum. In developing countries, where bovine tuberculosis is still enzootic, dogs can be infected by M. bovis by consumption of raw milk, or possibly raw meat or offal from affected cattle. It may be a potential risk for dogs living on farms that have tuberculosisinfected cattle. In dogs, tuberculosis caused by M. tuberculosis, which was reported to account for more than 65% of dog cases in France more than 30 years ago (Clercx et al., 1992), is clinically characterized by a pleura-pneumonia. Unfortunately, clinical signs, such as fever, weight loss, and coughing, are not specific. Infection by M. bovis more commonly induces a digestive form of tuberculosis.

In dogs, tuberculous lesions resemble sarcomatous lesions, rather than the typical tubercles, as caseation is rarely seen (Clercx et al., 1992). Atypical mycobacteria often gain entry via the skin and wounds, and so cause cutaneous signs, such as nodules and pyogranulomas. Human contamination from a M. tuberculosis-infected dog results from infective aerosols or contact with urine, saliva, or cutaneous lesions. Alimentary tuberculosis is the most likely result of M. bovis infection in dogs, making faecal excretion from affected dogs a possible zoonotic risk. Infection of dogs with other Mycobacterium spp. is rare and their zoonotic potential is still questioned. However, in immunocompromised patients, animal infections may be a potential source of human infection. M. genavense, a reported cause of a wasting illness in patients with AIDS, was isolated from a cervical lymph node from a dog with severe hind-limb weakness, and from tracheal tissue from a parrot with acute onset of a respiratory distress syndrome (Kiehn et al., 1996).

Diagnosis is a complex task, as the skin test is not very reliable in the dog. Any suspicion of a human case of tuberculosis in a household where pets are present, especially dogs, should lead to the clinical examination of the dog. The most consistent methods for the diagnosis of tuberculosis in dogs have been the histopathological examination of appropriate specimens, the isolation of the bacteria by culture (Aranaz et al., 1996), but more commonly and reliably PCR on bronchoalveolar lavage (Hackendahl et al., 2004). However, histopathology is performed usually after the death of the animal and microbiological diagnosis requires several weeks. The use of PCR has brought major improvement in the diagnosis of canine TB and reduces to a few days the time for identification of the organism (Aranaz et al., 1996). Infected dogs should be destroyed and not treated, as diagnosis is often late and treatment lasts for several months, with the great risk of selecting multidrug-resistant strains.

## Q fever

Caused by Coxiella burnetii, Q fever is mainly transmitted to humans and other mammals through inhalation of infectious particles. In nature, C. burnetii is maintained by a wildlifetick cycle. However, infection through tick bites has been reported for various species, including humans. Highly infectious dust from tick faeces deposited on animal skin and from dried placenta following parturition are major sources of *C. burnetii* infections in these animals and humans. Dermacentor, Rhipicephalus, and Amblyomma ticks are probably responsible for the transmission of C. burnetii among dogs and wildlife (Hibler et al., 1985). The primary reservoir hosts for C. burnetii are ticks, and vertical transmission (transovarial and transstadial) is common. Infection in domestic and wild carnivores has been reported from various areas of the world. In a survey of 1040 dogs in California, Williberg et al. (1980) showed a 53% antibody prevalence (agglutinin). In Nova Scotia, it was found that a high prevalence of Phase II antibodies were present in cattle, but also in cats (24.1% of 216 cats). None of the 447 dogs tested had antibodies. Such results could be associated to the lack of tick infection in Nova Scotia (Marrie et al., 1985). Following laboratory-induced infection, C. burnetii has been demonstrated in the blood of cats for up to 1 month, and in urine for 2 months.

The organism can be isolated frequently from the placenta of cattle, sheep, and goats.

In several instances, human infections resulted from exposure to parturient carnivores, as high concentrations of the organism are found in the products of conception. Laughlin et al. (1991) reported an outbreak in a family after exposure to a deer and infected pregnant dog. In late November 1989, seven members of a family from New Brunswick became ill with headache, fever, myalgia, fatigue, sweats, and a mild non-productive cough. Six of the seven family members had abnormal chest X-rays and a fourfold or more rise in Phase II antibody titre to C. burnetii antigen with immunofluorescent antibodies (IFA). A detailed history revealed that one family member shot a deer in early November and some of the deer liver was fed to the familv dog. One week later, the dog gave birth to pups; one was stillborn and two died within the 1st week of life. The pups were born under the bed of one of the family members. The children, who were present in the room at the time of the puppies' birth, became sick 10 days later. In this outbreak, it was strongly suspected that the dog was responsible for the outbreak. It was seropositive and C. burnetii was isolated from the dog's uterus. Similarly, Q fever pneumonia developed in all three members of one family 8-12 days after exposure to an infected parturient dog, which gave birth to four puppies that all died within 24h of birth (Buhariwalla et al., 1996). Because of the close contact between dogs and cats and their owners, pets can be considered as sentinel animals for the presence of C. burnetii in the household environment (Williberg et al., 1980).

Diagnosis of Q fever is based on culture of *C. burnetii*, but is rarely performed for safety reasons in the laboratory (inoculation of guinea-pigs, embryonated eggs, tissue cultures). One could consider PCR on biological products available only in very specialized laboratories. Diagnosis is mainly based on serology using IFA, ELISA, complement fixation, or microagglutination. No specific study has been conducted on treatment efficacy in domestic dogs and cats, but it is likely that tetracyclines and chloramphenicol would be effective, as in humans. Preventing farm dogs from having close contact with sheep, goats, or cattle is difficult, but farmers having Q fever outbreaks in their flocks or herds should be aware of the risk associated with their pets. Tick prevention and control is also important, especially in dogs.

#### Streptococcosis

In one report, recurrent group A beta-haemolytic streptococcus (*Streptococcus pyogenes*) pharyngitis was not eliminated until the family dog was treated (Mayer and VanOre, 1983). Canines being reservoirs of human pharyngitis is still controversial (Wilson *et al.*, 1995). A case of apparent transmission of *Streptococcus equi* subsp. *zooepidemicus* from an infected dog to a handler who subsequently developed severe systemic infection was recently reported (Abbott *et al.*, 2010). Characterization of the haemolytic streptococci isolated from both the patient and the dog, by phenotypic and molecular analysis, confirmed the canine and human isolates were identical.

#### Methicillin-resistant Staphylococcus aureus (MRSA)

In a survey performed among Australian veterinarians in 2009, small animal practitioners had a 4.9% prevalence (fivefold that of controls), and regression tree analysis clearly isolated equine veterinarians as well as dog and cat practitioners as groups at increased risk of carriage of MRSA (Jordan *et al.*, 2011). The high prevalence of concurrent MRSA colonization, as well as identification of indistinguishable strains in humans and pet dogs and cats in the same household, suggested that interspecies transmission of MRSA is possible (Faires *et al.*, 2009).

#### Zoonoses of the Genito-Urinary Tract

#### **Brucellosis**

Organisms of the genus *Brucella* are small, non-motile, Gram-negative coccobacilli capable

of causing disease in man, dog, cattle, sheep, goats, swine, and various wildlife species. Brucellosis in humans is most commonly a food-borne disease caused by Brucella melitensis, as seen in California (Chomel et al., 1994b). The most common source of human infection is unpasteurized milk products. Dogs can be infected by several species of Brucella, including *B. abortus* and *B. melitensis*, and play a role in the dispersion of these organisms between farms, potentially being a source of human contamination. Infection of dogs with *B. abortus* has been reported in experimental and field studies (Forbes, 1990). Evidence exists for transmission from cattle to dog by ingestion of infected reproductive tissues. Additionally, it seems likely that infected dogs can transmit B. abortus to naive cattle. At present, the zoonotic potential of B. abortus transmission between dog and man appears limited in most developed countries. Conversely, dogs are the main reservoir of B. canis, which is pathogenic to humans (Johnson and Walker, 1992; Kerwin et al., 1992). In domestic and wild canids, *B. canis* is transmitted primarily by ingestion or inhalation of aerosolized postabortion material, but venereal transmission is also reported (Johnson and Walker, 1992).

Human infection by B. canis is not common, but at least 30 human cases have been reported (Lum et al., 1985). In Argentina, an outbreak involved six persons (three children and three adults), and a bitch and three puppies which had close daily contact with the family (Lucero et al., 2010). The clinical symptoms of the index case led to an erroneous diagnosis and the infection would have gone undiagnosed if culture had not been positive. Symptoms of B. canis infection in humans are largely non-specific and include fever, splenomegaly, malaise, myalgia, headache, and anorexia (Lum et al., 1985). Septicaemia has been reported in 50% of patients (Rousseau, 1985). Though most cases respond well to antibiotic therapy, as many as 3% of treated patients may die from endocarditis or other complications (Rousseau, 1985).

In dogs, *B. canis* infection is characterized by prolonged bacteraemia and reproductive failure in both males and females. Transient lymphadenopathy and fever are occasionally detected in early stages of infection (Johnson and Walker, 1992). In the pregnant bitch, *B. canis* causes embryonic or foetal death, or abortion, by colonizing the placental epithelial cells. Live-born puppies infected *in utero* do not usually survive to weaning (Carmichael and Greene, 1990). In the male dog, *B. canis* causes epididymitis and infertility as a result of abnormal spermatogenesis (Johnson and Walker, 1992). In both genders, infection is largely asymptomatic and often remains undetected unless the animal is bred. Occasionally complications arise, including discospondylitis, uveitis, meningitis, glomerular nephritis, and draining skin lesions.

A diagnosis of brucellosis can be made by either blood culture or serology. In the case of serology, specific *B. canis* antigen should be used, as serological tests for diagnosis of ruminant or swine brucellosis do not cross-react with this antigen (Polt *et al.*, 1982). Treatment is based on the use of doxycycline and an aminoglycoside (streptomycin, gentamycin, or netilmicin) for 4 weeks followed by doxycycline (200 mg per day) and rifampin (600–900 mg per day) orally for 4–8 weeks (Tan, 1997).

#### Leptospirosis

Leptospirosis is mainly a water-borne disease and rodents are major reservoirs. Man is an accidental host, becoming infected through occupational or recreational exposure. Leptospirosis has a worldwide distribution, but human cases are more frequently reported from the tropics, such as Hawaii for the United States, where the average annual incidence is 1.08 per 100,000 population, while it is 0.05 per 100,000 population for the United States as a whole (Sasaki *et al.*, 1993).

The etiological agents of leptospirosis belong to the more than 200 pathogenic serovars within the 23 serogroups of *Leptospira interrogans* (Andre-Fontaine *et al.*, 1994). Many of these serovars are capable of causing disease in humans and dogs, but until recently the main serovars involved in zoonotic transmission between canids and humans were *L. canicola* and *L. icterohaemorrhagiae* (Farr, 1995). More recently, canine outbreaks caused by *L. pomona* and *L. grippothyphosa* have been reported in Europe (Andre-Fontaine *et al.,* 1994) and in the United States, and to a lesser extent by *L. australis, L. automnalis,* or some other serovars.

Dogs are the natural carrier host for L. canicola, but can also be infected with various other serovars and will shed these organisms in their urine for up to several weeks. Humans can become infected through licking from, or when petting, an infected dog. Recently, many cases of leptospirosis have been reported in dogs in the United States caused by L. grippothyphosa, especially in the north-eastern states. The reservoirs are more likely to be racoons, opossums, and skunks. The specific role of dogs as source of human infection is not well quantified, but is reported to be high. Human infection with L. icterohaemorrhagiae is associated with exposure to infected dogs and is the most commonly diagnosed leptospiral infection in humans (Heath and Johnson, 1994). As most dogs are vaccinated against L. canicola and L. icterohaemorrhagiae in developed countries, suspicion of leptospirosis is often ruled out in a differential diagnosis. However, dogs may be infected by other serovars, and be potential carriers and shedders of all serovars. In California, 10% of 61 leptospirosis cases in humans over a 20-year period resulted from pet contact (Meites et al., 2004).

The course of infection caused by exposure to a leptospiral agent is largely dependent on host adaptation of the serovar. Infection of an animal with its species' host-adapted serovar usually results in a mild disease state and high likelihood of development of a chronic carrier and shedder state. Such individuals represent reservoir or maintenance hosts. Infection with a non-host-adapted serovar typically causes severe acute disease characterized by hepatitis, haemolytic crisis, and organ failure (Heath and Johnson, 1994). In dogs, leptospirosis can range from an acute septicaemia with haemolytic anaemia, hepatorenal failure, uncontrollable vomiting and bloody diarrhoea, to a subacute form with fever and jaundice, or to milder forms with chronic nephritis.

In humans, after an incubation period of 7–12 days, most persons will have a subclinical infection or anicteric febrile disease, often misdiagnosed as influenza. In its initial febrile phase, which usually lasts for 4-7 days, fever, headache, myalgia, conjunctivitis, nausea, and vomiting are commonly seen (Heath and Johnson, 1994). In severe cases, by the end of the 1st week, jaundice and renal failure may begin. By the 3rd week, severe icterus with high levels of bilirubin is observed, usually associated with severe glomerulonephritis or interstitial nephritis. The mortality rate may reach 10-20%. Leptospira spp. may be isolated from the patient's blood or cerebrospinal fluid during the 10 days of infection, or the urine after 21 days, and identified by dark-phase microscopy or culture. Recent molecular techniques, such as PCR or immunoblotting may reduce the time for diagnosis, as culture may require several weeks, but seems to be less sensitive than serological diagnosis (Levett, 1999). Laboratory diagnosis is still mainly based on serology, especially micro-agglutination. Agglutinins will appear between the 6th and 12th days of illness. A specific diagnosis is usually based on the demonstration of a fourfold rise in antibody titre. Several serological tests have been developed, including ELISA or IFA. Leptospira spp. are very sensitive to penicillin G and doxycycline, which are the most effective antibiotics in dogs and humans, especially when administered in the early phase of the disease. Prevention is based on rodent control and exposure reduction, as well as dog vaccination.

#### Vector-Borne Zoonoses

Dogs are not usually the main source of human infection for vector-borne zoonoses. However, their role cannot be neglected as they either bring or attract the various vectors that can bite humans (fleas, ticks, phlebotomes) into the human environment, or can be a source of infection on which vectors feed and further transmit infectious agents to humans.

#### Lyme borreliosis

Lyme disease is a multisystemic, tick-vectored, zoonotic disease associated with infection by spirochetes of the genus *Borrelia* (Levine,

1995). The disease was first characterized in the mid-1970s during an investigation of an outbreak of arthritis near Old Lyme, Connecticut (Spach et al., 1993). Though the name Lyme disease was new, the syndrome was soon recognized to be similar to erythaema chronicum migrans and acrodermatitis chronica atrophicans, disease entities recognized in Europe as early as 1883 (Levine, 1995). Borrelia burgdorferi is the etiological agent of Lyme disease in the United States, while B. garinii and B. afzelii are also associated with borreliosis in Europe (Saint-Girons et al., 1994). Lyme disease is the most reported vector-borne disease of humans in the United States. Lyme disease is common in children, with about one-fourth of all reported cases occurring in children < 14 years of age (Sood, 1999). During 1992-2006, a total of 248,074 cases of Lyme disease was reported to CDC by health departments in the 50 states, the District of Columbia, and US territories. The annual count increased 101%, from 9908 cases in 1992 to 19,931 cases in 2006. During this 15-year period, 93% of cases were reported from 10 states (Connecticut, Delaware, Massachusetts, Maryland, Minnesota, New Jersey, New York, Pennsylvania, Rhode Island, and Wisconsin). Incidence was highest among children aged 5-14 years, and 53% of all reported cases occurred among males (Bacon et al., 2008). For comparison, the *Borrelia* infestation rate of Ixodes ricinus is 7%, with wide disparity between administrative districts. Prospective work in 1999-2000 established the estimated incidence of Lyme disease (9.4/100,000) and of neuroborreliosis (0.6/100,000) in France. Incidence was higher in certain regions, such as Alsace, with an estimated Lyme disease incidence at 86 to 200/100,000 inhabitants and neuroborreloisis at 10/100,000 (Blanc, 2009). Infection with B. burgdorferi has been demonstrated in several mammalian and avian species (Barbour and Fish, 1993; Levine, 1995). However, as Lyme disease is not a reportable disease in animals, reliable incidence data are not currently available for wild and domestic species.

The enzootic cycle of Lyme disease does not normally include humans or domestic animals (Mather *et al.*, 1989). Rather, maintenance of *B. burgdorferi* in the environment is dependent on a wildlife reservoir and a transmission vector. B. burgdorferi is exceptional amongst Borrelia spp. in that it is capable of infecting a wide range of tick and vertebrate hosts. Thus, different animals and vectors are responsible for perpetuating *B. burgdorferi* in the different geographic regions in which Lyme disease is endemic. Several ticks of the genus *Ixodes* have been demonstrated to be competent in transmitting Lyme borreliosis. In the eastern and north-central United States I. scapularis is the main vector (more than 50% of the ticks can be found infected), while in the Pacific states transmission is primarily via I. pacificus (of which 1-6% are infected). In Europe *I. ricinus* is the main vector (Lane *et al.*, 1991; Barbour and Fish, 1993). Transovarial passage of B. burgdorferi in Ixodes ticks is only 1-5% (Lane *et al.*, 1991), suggesting that ticks act as vectors rather than as reservoirs for the spirochete. In the north-eastern United States, it has been shown that the white-footed mouse. Peromyscus leucopus, is the primary reservoir of B. burgdorferi (Mather et al., 1989; Levine, 1995). Mice generally become infected when fed upon by nymph stage I. scapularis, which acquire spirochetes during their larval feeding (Genchi, 1992). Adult I. scapularis feed primarily on white-tailed deer (Odocoileus virginianus). In northern California the life cycle of *B. burgdorferi* often involves two tick species. I. neotomae is responsible for maintaining the spirochete in the dusky-footed wood rat (Neotoma fuscipes), the primary reservoir in that region (Lane et al., 1991). However, the host range of *I. neotomae* is narrow, so I. pacificus is the vector responsible for spreading B. burgdorferi infection to other species including humans and dogs. All three stages of ticks can be found on humans and domestic animals (Kazmierczak and Sorhage, 1993). In Europe, Lyme borreliosis is mainly transmitted by I. ricinus (Genchi, 1992). The infection rate in these ticks varies from 4% to 40%.

A major concern of any zoonosis of the dog is the potential that contact with canines will increase the likelihood of humans contracting the disease. Studies have indicated that dogs are competent reservoirs of *B. burg-dorferi* (Mather *et al.*, 1994). Thus, naive ticks that feed on infected dogs are likely to become infected. Such ticks are then capable of infecting other vertebrates including

humans. By introducing infected ticks into the human environment, dogs are capable of increasing dog owners' exposure to *B. burgdorferi*. Estimates of the prevalence of antibody to *B. burgdorferi* in dog populations in Massachusetts offers a sensitive, reliable, and convenient measure of the potential risk to people of *B. burgdorferi* in the environment (Lindenmayer *et al.*, 1991). Risk factors for canine seropositivity may directly or indirectly illuminate certain aspects of the epidemiology of human Lyme disease.

Dogs infected with *B. burgdorferi* may manifest some of the clinical signs which are common in humans, including acute onset of recurrent lameness, fever, lethargy, and inappetance. Other symptoms that occur with lower frequency include generalized lymphadenopathy, CNS disorders, uveitis, renal lesions, and cardiac disease (Kazmierczak and Sorhage, 1993).

In humans, Lyme disease manifests with a variety of dermatologic, rheumatologic, cardiac, and neurologic abnormalities (Steere, 1989; Levine, 1995). The CDC case definition of Lyme disease includes the characteristic erythema migrans (EM) lesion (> 5 cm in diameter) or laboratory confirmation of B. burgdorferi infection, and at least one of the objective clinical signs of the disease (CDC, 1990). Erythema migrans is virtually pathognomonic when it occurs, but is only detected in approximately 60% of patients (Steere, 1989). In the early stages of the disease, EM is often accompanied by muscle pain, headache, and fatigue. Leukocytosis, increased RBC sedimentation rate, and haematuria may also occur. In Europe, the manifestations of Lyme borreliosis are slightly different, with nervous-system involvement being more common, especially facial palsy, meningitis, and polyradiculoneuritis, and are more common in children (17-38% of cases) than in adults (Sood, 1999). Chronic arthritis has been reported in up to one-third of German children with Lyme arthritis (Sood, 1999).

Diagnosis is mainly based on serological assays. A 'two-step approach' has been widely adopted and has improved the specificity of the diagnosis. It is based on an enzyme immunoassay or indirect immunofluorescence assay followed by an immunoblotting assay (Western blot). Detection of IgM is investigated in early stages of the infection. Borreliosis is resolved in most patients with a 10-21-day course of treatment with doxycycline ( $100 \text{ mg} \times 2 \text{ per day}$ ) or amoxicillin  $(2g \times 3 \text{ per day})$  orally (per os). Intravenous ceftriaxone (2g per day for 2-3 weeks) may be indicated if the infection is not detected in the early stages or appears refractory to initial treatment protocols (Steere, 1989; Levine, 1995). For reasons that are poorly understood, some individuals are unable to overcome B. burgdorferi infection. These patients may experience chronic peripheral nervous system and CNS abnormalities including depression, fatigue, sleep disorders, and memory loss for months to years following the initial infection (Barbour and Fish, 1993).

Prevention of Lyme disease in humans and domestic animals relies largely on minimizing exposure to ticks. Tick-infested areas should be avoided whenever possible. When travelling in areas of high tick density, exposure can be minimized by wearing long-sleeved shirts and long pants tucked into one's socks. Tick repellents and acaricides are available for human and animal use. Humans should inspect themselves and their pets regularly for ticks, and carefully remove them as soon as possible after contact (Barbour and Fish, 1993; Kazmierczak and Sorhage, 1993). Removal of ticks within 48h of attachment has been shown to significantly decrease the likelihood of transmission of B. burgdorferi from an infected tick (Shih and Spielman, 1993). In addition to vector control, the other method of preventing borreliosis in dogs and humans is by vaccination. There are currently various vaccines available for use in dogs in the United States including inactivated whole-organism bacterins, while the others are recombinant vaccines based on either OspA and/or OspC proteins (Levine, 1995). Concern about residual pathogenicity has precluded development of whole-cell vaccines for human use (Barbour and Fish, 1993).

#### Ehrlichiosis/Anaplasmosis

Organisms of the genus *Ehrlichia* and *Anaplasma* are pleiomorphic, obligate intracellular bacteria of the family *Rickettsiaceae*  that parasitize the phagosomes of mononuclear or polymorphonuclear leukocytes (Eng et al., 1990; Anderson et al., 1991). Human ehrlichioses are recently recognized tick-borne infections (McQuiston et al., 1999). In 1986, a clinically novel form of human monocytic ehrlichiosis (HME) was described and shown to induce an E. canis-reactive humoral reaction (Maeda et al., 1987). The advent of taxonomic determination based on 16S rRNA gene sequencing led to the discovery that E. canis-like human ehrlichiosis was actually caused by a previously undescribed species, subsequently named E. chaffeensis (Anderson et al., 1991). Evidence of human infection with E. canis, the cause of canine monocytic ehrlichiosis, has also been reported (Perez et al., 1996). Finally, another agent causing granulocytic ehrlichiosis in dogs, E. ewingii, was reported to cause human illness in four patients (Buller et al., 1999).

The main vector of E. chaffeensis and E. ewingii is the Lone Star tick, Amblyomma americanum, and the dog tick, Dermacentor variabilis (Walker and Dumler, 1996). From 1986 to 2006 more than 2300 human cases of HME have been reported to the CDC, mainly from the south-eastern and south-central United States (Ismael et al., 2010). In 1990, canine and human infections with granulocytic ehrlichiae were discovered in Minnesota and Wisconsin (Bakken et al., 1994). Human granulocytic anaplasmosis (HGA), formerly human granulocytic ehrlichiosis (HGE) is caused by an organism closely related to E. equi and E. phagocytophila (Chen et al., 1994), now known as Anaplasma phagocytophilum (Nicholson et al., 2010). The main vector of HGA agent is *I. scapularis* in the mid-western and north-eastern United States (Walker and Dumler, 1996). Since first identified, more than 3000 human cases of HGA have been reported to the CDC, mainly from the northeastern and upper mid-western United States (Ismael et al., 2010). The zoonotic nature of human ehrlichioses and anaplasmosis is supported by reports of natural infections with the same species in dogs, deer, horses, and rodents. Dogs are likely to contribute to the enzootic cycle and human infection. Dogs can also become infected with E. chaffeensis in experimental (Dawson and Ewing, 1992) and

natural conditions (Breitschwerdt *et al.*, 1998). In dogs, disease caused by infection with *A. phagocytophilum* is typically characterized by acute onset of fever, depression, myalgia, anorexia, lameness, and reduced platelets. In people, *A. phagocytophilum* infection is characterized by fever, headache, lethargy, myalgia, elevated liver function enzymes, and reduced platelets. Human fatalities can occur, although reportedly in <1% of cases, and usually in association with other opportunistic infections (Nicholson *et al.*, 2010).

Canine monocytic ehrlichiosis, caused by *E. canis*, has been described throughout most of the world but is particularly prevalent in tropical and subtropical regions (Eng and Giles, 1989). This infection is mainly transmitted by Rhipicephalus sanguineus. In dogs it manifests, in the acute phase, with fever, depression, anorexia, and weight loss. Typical laboratory findings include thrombocytopaenia and hypergammaglobulinaemia (Eng and Giles, 1989). Though most dogs recover uneventfully, some progress to a subclinical stage characterized by persistent haematological abnormalities and high antibody titres to E. canis (Codner and Farris-Smith, 1986). Chronic ehrlichiosis, characterized by pancytopaenia and bone marrow hypoplasia, may develop weeks to years later. This chronic form has a high fatality rate attributed to haemorrhages and secondary infections (Eng and Giles, 1989).

Canine granulocytic ehrlichiosis, caused by *E. ewingii*, was first described in a dog from Arkansas (Ewing *et al.*, 1971) and has been reported since then from dogs in several parts of the south-eastern United States. In dogs, *E ewingii* infection is usually milder than *E. canis* infection and responds to treatment with tetracycline (Buller *et al.*, 1999). In the series of cases reported by Buller *et al.* (1999), all four patients had been exposed to ticks and had had contact with dogs shortly before the onset of symptoms. One of the patient's dogs had asymptomatic infection, suggesting that dogs could act as a reservoir for *E. ewingii*.

Human monocytic and granulocytic ehrlichioses are nearly indistinguishable and are characterized by one or more of the following symptoms: fever, headaches, myalgia, chills, anorexia, rash in 20% of the patients (for HME, less common for HGA), leucopaenia, thrombocytopaenia, anaemia, hypertension, coagulopathy, renal failure, pancytopaenia, hepatocellular injury, and elevated serum hepatic aminotransferase levels (Walker and Dumler, 1996; McQuiston *et al.*, 1999; Ismael *et al.*, 2010). The severity of the disease ranges from asymptomatic seroconversion to fatal infection. Case-fatality rates that were as high as 5% for HME and 10% for HGA (Dumler and Bakken, 1995) have now declined to less than 2% (HME) and 1% (HGA).

Human and animal ehrlichioses are mainly diagnosed by indirect immunofluorescence assay, although PCR assays are increasingly used (McQuiston *et al.*, 1999; Ismael *et al.*, 2010). Treatment of infections caused by *Ehrlichia* spp. in dogs is mainly based on the use of doxycycline at 100 mg twice a day for 5–7 days (Tan, 1997). Prevention is based on the same measures as reported for Lyme disease.

## Spotted fever group rickettsioses

Spotted fever group *Rickettsiae* have been described throughout the world (Azad and Beard, 1998). Though the organisms are closely related, each causes a serologically and pathologically distinct disease. Most rickettsioses are considered zoonotic. Rocky Mountain spotted fever is caused by *Rickettsia rickettsii*, and occurs in the United States, Canada, Mexico, and parts of Central and South America. In Japan, Oriental spotted fever is caused by *Rickettsia conorii* causes Boutonneuse fever in several Mediterranean nations, southern Africa, and the Middle East (Walker and Fishbein, 1991).

#### Rocky Mountain spotted fever

Rocky Mountain spotted fever (RMSF) is a tick-borne rickettsial disease caused by *R. rickettsii*, which affects several vertebrate species including humans and dogs. R. *rickettsii*, the most pathogenic of all known rickettsial species, resulted in the death of 23% of infected persons in the pre-antibiotic era (Walker *et al.*, 2008). It is known to be transmitted in the United States by three tick species: *Dermacentor variabilis* (American dog tick), *D. andersoni* (Rocky Mountain wood tick), and more recently *Rhipicephalus sanguineus* (brown dog tick) in Arizona and Northern Mexico. In South America, *R. rickettsii* is transmitted by two other tick species, *Amblyomma cajennense* (Cayenne tick) and *A. aureolatum* (golden dog tick). RMSF was first reported in 1896 when cases were identified in Idaho in the Snake River valley and in the Bitter Root valley of western Montana (Dalton *et al.*, 1995).

Howard T. Ricketts first established the identity of the bacteria-like infectious particles seen in tick tissues and demonstrated the competence of the wood tick, Dermacentor andersoni, in acquiring and transmitting the infectious agent. Beginning in the 1930s, RMSF started to be reported from eastern states (Dalton et al, 1995). RMSF is found all over the United States, the largest number of cases being reported from the south-eastern, mid-western, and south-central states. The disease also exists in Canada, Mexico, Central America, and parts of South America (Colombia and Brazil). The natural history and distribution of RMSF in the United States are associated with the ecology of two ticks (Hibler et al., 1985). D. andersoni is the principal vector of disease in the western United States from the Cascade to the Rocky Mountains. Its larvae and nymphs feed on small mammals; the adults infest larger mammals. The wood tick is active primarily in the spring and early summer, when the disease incidence peaks. In the south-eastern and eastern United States, the American dog tick, D. variabilis, is the main vector. Its larvae and nymphs feed on wild rodents; adults feed on larger feral mammals, dogs, and humans. In the eastern United States, the Lone Star tick, A. americanum, is implicated in human infection. More recently, Rhipicephalus sanguineus, the brown dog tick was shown to be an efficient vector of R. rickettsii in Arizona and northern Mexico (Nicholson et al., 2010).

The rickettsiae are released from the salivary glands of feeding adult ticks during their 6–10h of attachment. *R. rickettsii* 

initially infects the epithelial cells of the tick midgut, multiplies there, enters the haemocoel, and then invades all tick tissues, including the salivary glands and the ovaries. The organism can be found in the tick haemocytes as early as 3-5 days after the infective meal. When generalized infection occurs, all tick tissues can become infected within a 7-10-day period after feeding on a rickettsiemic animal. Uninfected nymphs and adults may become infected with R. rickettsii when they feed on animals concurrently with infected nymphs or adults. Ticks mate while feeding. Female ticks transmit the infection through the eggs, but transfer through male spermatozoa is not efficient during mating (McDade and Newhouse, 1986). Acquisition of infection by ticks is limited to the rather short period of high rickettsaemia (often 4-5 days only) in the small rodents. The extensive range of mammals that are seropositive for R. rickettsii reflects the generalized feedings habits of the known tick hosts of R. rickettsii. The American dog tick (D. variabilis) feeds mainly on dogs for the adult form, but will also feed on many other domestic and wildlife mammals (cattle, sheep, horses, deer, raccoons, opossums, coyotes, foxes). Larvae and nymphs feed on various rodents, such as chipmunks, ground squirrels, voles, and rabbits. Rhipicephalus sanguineus, a major vector in Mexico, is primarily associated with domestic dogs. Humans are an incidental host of the adults of all of these tick species, and therefore do not contribute to the transmission cycle (McDade and Newhouse, 1986). In both humans and dogs, the level of rickettsaemia is low, and they do not serve to infect new ticks. Larvae and nymphs usually do not feed more than once before moulting. Adult female ticks feed once before laying eggs, after which they die, and only adult males feed repetitively. Dogs inoculated with 1000-10,000 egg infective doses of virulent R. rickettsii developed a rickettsaemia that was detectable as early as 4 days after inoculation and as late as 10 days (Norment and Burgdorfer, 1984). In the same experiment, these authors showed that a very limited number of ticks became infected after feeding on inoculated dogs.

No rickettsaemia has been observed in dogs infected with *R. rhipicephali* or *R. montana,* two non-pathogenic rickettsiae.

In dogs, rickettsaemia lasts only for a few days. Serologic information obtained since the 1930s indicated that dogs could be infected, but it is only since the late 1970s and early 1980s that clinical reports concerning naturally occurring RMSF in dogs have been made (Keenan et al., 1977). Symptoms of RMSF vary considerably in dogs. Usually, fever (39°C-41°C), anorexia, vomiting, diarrhoea, and depression can occur within 2-3 days of tick attachment (Greene et al., 1985). Conjunctivitis, mucopurulent oculo-nasal discharge, and non-productive cough are often present. Weight loss, dehydration, lymphadenopathy, and myalgia may occur, as well as joint tenderness. Abdominal tenderness or paralumbar hyperaesthesia can be observed. Early skin lesions include oedema and hyperaemia (lips, pinnae, prepuce, scrotum), followed by cutaneous petechiae and ecchymoses (only in 20% of the dogs, whereas it is in the majority of human cases), epistaxis, and scleral injection. Haemorrhages are limited to the mucosae, rather than involving the skin. Necrosis of skin of the extremities has been seen as a complication of RMSF in dogs. Ocular lesions are characterized by subconjunctival haemorrhage, hyphaema, anterior uveitis, retmal petechiae, and focal retinal oedema (Davidson et al., 1989). Neurologic abnormalities, such as vestibular deficits, abnormal mental status, nystagmus, head tilt, circling, and incoordination are also observed. Haematologic abnormalities include anaemia (normocytic, normochromic); thrombocytopaenia; platelet counts of less than 75,000 cells per ml (normal: 200,000-500,000), and mild leukopaenia (at onset of fever). These are followed by leukocytosis (> 20,000) with a left shift (normal: 6000–17,000). Biochemical abnormalities include increased glucose concentration, increased serum aspartate and alanine transaminases and alkaline phosphatase activity, and hypoproteinaemia.

In humans, 4–14 days after a tick bite, the patient suffering typical RMSF has an acute onset of fever, malaise, headache, and myalgia, followed 1–15 days after the onset of illness by a petechial rash. Vomiting can be seen in 60% of the cases. The rash first appears as macules on the wrists and ankles, and subsequently spreads to involve the trunk, face, palms, and soles. These cutaneous lesions often develop papular, petechial, or purpuric features. Acute renal failure, coagulopathy, and cerebral oedema are common complications. Mortality, as high as 30% in the pre-antibiotic era, has declined below 1%, but is higher in some parts of the United States, especially in Arizona. The US incidence of RMSF cases reported to the Centers for Disease Control and Prevention has increased from fewer than 500 reported cases in the early 1990s to 2288 cases in 2006 and 2106 cases in 2007, the highest recorded levels in more than 80 years of national surveillance for this disease (Walker et al., 2008). RMSF also seems to be re-emerging in several countries in Latin America. The frequency of reported cases of RMSF is highest among males, American Indians, and people aged 50–69.<sup>1</sup> It is a seasonal (summer) disease, and individuals with frequent exposure to dogs and who reside near wooded areas, or areas with high grass, may be at increased risk of infection. Children up to 9 years of age and American Indians have an increased risk of fatal outcome from RMSF.

Diagnosis of the infection is based on isolation of the agent by inoculation to guinea-pigs, on cell cultures, by direct immunofluorescence on skin biopsies, or by serological tests (IFA, ELISA, microagglutination) (Greene *et al.*, 1993). Testing by PCR of 17 KDa antigen has been developed more recently. In dogs, serodiagnosis based on detection of both IgM and IgG is also useful to identify acute infection (Breitschwerdt *et al.*, 1990).

The treatment of choice is tetracyclines (22 mg per kg every 8h, per os; or chloramphenicol: 15–20 mg per kg, every 8h, per os). Breitschwerdt *et al.* (1997) showed that prednisolone at anti-inflammatory or immunosuppressive dosages, in conjunction with doxycycline, does not potentiate the severity of *R. rickettsii* infection in dogs (rickettsaemia was prolonged at immunosuppressive dose).

#### Mediterranean spotted fever or Boutonneuse fever

Boutonneuse fever, also called Mediterranean spotted fever (MSF), was first described by Connor and Bruch in Tunis in 1910. It is an acute infectious disease caused by R. conorii (Font-Creus et al., 1985). The habitual reservoir and dominant vector is the brown dog tick, R. sanguineus, which very rarely feeds on humans. In 1930, Durand and Conseil produced the disease in man by injecting suspension of R. sanguineus taken from a dog. The disease is endemic along the Mediterranean coastline. The disease is also endemic in much of Africa, the Middle East, and the Black and Caspian Seas. It is also the most common rickettsial disease in South Africa (Rovery and Raoult, 2008). In South Africa, the dog ticks Haemaphysalis leachi and R. sanguineus are the principal vectors of human infection. An increase in human cases has been reported in the last decade in several Mediterranean countries (Rovery and Raoult, 2008). In Mediterranean countries, dogs seem to play an important role in the epidemiology of the disease as amplifiers of the reservoir and vector, the brown dog tick, in a domestic or peridomestic cycle in urban or peri-urban areas. They also bring infected ticks into the vicinity of humans.

Dogs are often considered to be the main source for infecting ticks, yet there are no quantitative data concerning susceptibility of dogs to this agent. Senneville et al. (1991) reported the case of a 53-year-old man who presented a severe form of MSF 2 months after holidaying on the French Riviera. When tested, the pet dogs were found seropositive with very high titres. When three brown dog ticks were found on the dogs a few months later, these were cultured and R. conorii was identified. Similarly, a few cases of RMSF were reported in The Netherlands, as the infection with *R. conorii* had been transmitted through dogs that had stayed in Mediterranean countries and had carried ticks to The Netherlands (Ruys et al., 1994). The increase in human cases is related to the dispersion of *R. sanguineus* by dogs from southern Europe to more northern areas, and also to the progressive adaptation of R. conorii to new tick species such

as Dermacentor marginatus or D. reticulatus. Dogs are exposed to infection, and, although clinical signs and symptoms have not been reported, they can be rickettsiemic. Adult dogs can carry R. conorii without clinical signs, but they do not transmit it to their offspring. In Spain, Delgado and Carmenes (1995) and Segura-Porta et al. (1998) found that 23.4% of 308 dogs and 26.1% of 138 dogs tested, respectively, had significant antibody titre to *R. conorii*. The frequency of seropositive dogs increased during the summer months. Dogs from rural areas or heavily infested by ticks had a higher seroprevalence. It has been suggested that dogs could be used as sentinels to monitor the distribution of this zoonosis. In other parts of the world, small rodents upon which infected ticks feed are the amplifiers on the infection. It is suspected that in the Mediterranean basin lagomorphs could play the role of amplifiers in the wildlife cycle. In a sero-survey, 76.5% of the wild rabbits tested in Salamanca Province, Spain, had antibodies

(Ruiz-Beltran et al, 1992). In humans, MSF is characterized by a primary lesion at the site of the tick bite. It is a small reddish ulcer covered by a small black scab, called 'tache noire', which may last throughout the course of the illness. Regional lymphadenopathy is often seen. Fever appears usually 5–7 days after the tick bite and is associated with severe cephalagia, muscular, and joint pain. A generalized eruption, at first macular and then maculopapular, appears the 4th or 5th day of the fever and lasts about 1 week. However, presence of multiple eschars was recently reported (Rovery and Raoult, 2008). Mortality is usually low, but an increased mortality, with a case fatality rate as high as 32% in Beja, Portugal, was recently reported (Rovery and Raoult, 2008). In a study of 227 cases in Spain, Font-Creus et al. (1985) reported a high fever and a generalized maculopapular rash in all patients. The 'tache noire' was seen in 73% of the cases, as well as myalgia. Other common signs were headaches (69%), conjunctivitis (32%), hepatomegaly (44%), and splenomegaly (19%). Contact with dogs was confirmed in 92% of the 170 cases analysed. Seventy-two per cent of the cases were living in urban areas.

The epidemiology of MSF is determined by the biology of the tick and results in a consistent seasonal peak. Immature stages (larvae, nymphs) are generally the source of human contamination during the summer, while adult ticks are mainly active during the spring. The monthly distribution of human cases shows that the apparition of the disease parallels the maximal activity of the immature stage of *R. sanguineus* (Raoult *et al.*, 1992). R. conorii is transmitted transovarially from generation to generation. In their study, Raoult et al. (1992) found that incidence was positively correlated with average temperatures during spring and summer of the preceding year, and negatively correlated with the number of days with frost during the preceding year. Raoult et al. (1993) also reported interesting data concerning prevalence of MSF and prevalence of infected ticks in the Marseille area. In northern Marseille, the incidence of hospitalized patients with MSF was 24.2 per 100,000 persons compared with 9.8 and 8.8 per 10<sup>5</sup> for central and south-eastern Marseille. Seroprevalence in blood donors, tested by microimmunofluorescence and confirmed by Western blot assays was higher in the northern area than in central and southeastern Marseille (6.7% versus 3.6 and 2.4). They indicated that this higher prevalence may be related to a greater tick exposure due to a higher number of dogs (32.6 per 100 inhabitants versus 28.4 and 27.2 per 100, respectively). About 9-15% of the ticks were infected in the various areas. For human infection, the brown tick needs to be attached for at least 20 h. Dogs in northern Marseille are more frequently parasitized by ticks (51.4%) than in the two other areas (43.5% and 40%, respectively). Parasitized dogs are present in microfoci. In northern Marseille, a large percentage of the population has a low income and more than 25% are unemployed. It is therefore possible that such negative socio-economic factors negate the effects of adequate hygiene facilities on personal hygiene. The diagnosis of infection is usually performed by either isolation of the infectious agent (not done in regular practice) or serologically by microimmunofluorescence and Western blot assays (Teysseire and Raoult, 1992). The treatment is based on the use of tetracyclines (Doxycycline

100–200 mg per day for 7–15 days) and chloramphenicol. Several other rickettsial spotted fevers have been reported from various parts of the world, but no data are available on the role of dogs in their epidemiology.

#### Plague

Plague, caused by Yersinia pestis, is an endemic disease of rodents in Asia, central and southern Africa and Madagascar, some areas of South America (Peru, Bolivia, Brazil), and the western United States. It is maintained in nature by a flea-rodent cycle of transmission. In man, bubonic plague results from a flea bite, usually from a rodent flea, but sometimes from a cat or dog flea. In humans, infection with Y. pestis occurs through the bite of infected fleas, contact with bodily fluids of infected animals, or rarely through inhalation of aerosolized respiratory droplets of infected animals or other humans (Crook and Tempest, 1992). Inhalation infection results in pneumonic plague, the form associated with the greatest mortality. In the dog, infection is most likely to occur as a result of flea bites or ingestion of an infected rodent (Orloski and Eidson, 1995)

In humans, clinical forms of plague present as bubonic, septicaemic, or pneumonic. Clinical signs for the bubonic form typically include fever, myalgia, lymphadenopathy (buboe), nausea, and vomiting (Crook and Tempest, 1992). The incubation period ranges from several hours to approximately 1 week. In dogs, plague is usually a mild disease, characterized by a moderate fever, lethargy, and enlarged lymph nodes (Orloski and Eidson, 1995). In endemic areas, plague antibody prevalence in pet dogs is usually low. In the United States, prevalence is less than 1% in pet dogs (Chomel et al., 1994a), whereas rates of 4% up to 16% have been reported in dogs, especially on Native American Reservations (Chomel et al., 1994a, Barnes and Poland, 1983) or in Africa (Kilonzo et al., 1992).

The frequency with which plague is transmitted from dog to human has not been thoroughly examined (Orloski and Eidson, 1995). Four cases of acquiring plague from skinning wild canids were documented between 1970 and 1993. Though 12 cases of human plague during this period were attributed to direct contact with an infected domestic cat, no analogous cases were confirmed following interaction with an infected dog (Craven et al., 1993). As with other arthropodborne diseases, dogs may introduce vectors infected with Y. pestis into the human environment and thereby increase the likelihood of humans contracting plague. More recently, human cases of plague were associated with sleeping with a pet dog (Chomel and Sun, 2011; Gould et al., 2008; CDC, 2011). The plague bacillus is very sensitive to streptomycin, but tetracycline and doxycycline are also very effective. Major concern has been raised with the emergence of multi-resistant plague bacilli from Madagascar (Galimand et al., 1997). Dogs pose a risk to humans by transporting fleas and flea-infested animals or their carcasses into or around the home. It is important that dogs and cats that roam outside be treated with appropriate insecticides to kill fleas.

## Other Uncommon Bacterial Zoonoses

#### Anthrax

Dogs are not very susceptible to anthrax and usually develop a subclinical or chronic form of anthrax, with moderate fever, pharyngeal and lingual oedema, and enlarged lymph nodes (McGee *et al.*, 1994). Direct infection of humans from dogs could potentially occur through a bite.

#### Chlamydiosis

*Chlamydophila psittaci*, the agent of psittacosis/ornithosis in humans, is an obligate intracellular parasite that is capable of infecting a wide range of domestic and wild mammals and birds (Arizmendi *et al.*, 1992). In humans, *C. psittaci* infection is seen most often in exotic pet bird owners and poultry industry workers. Reports of natural and experimentally induced chlamydiosis in dogs are rare. C. psittaci has been isolated in England from the faeces of a dog that had ingested the carcasses of birds known to be infected with the same agent (Fraser and Norval, 1969). Chlamydial conjunctivitis has been described in dogs (Krauss et al., 1988). Additionally, experimental inoculations of dogs with the chlamydial agent of ovine polyarthritis support the notion that dogs are capable of supporting chlamydial infections (Maierhofer and Storz, 1969). Seroprevalence of canine chlamydiosis has not been examined in the United States. However, serosurveys have been conducted in Germany (Werth et al., 1987) where 20% of the dogs tested had C. psittaci antibodies, and in Japan (Fukushi et al., 1985), where 9% of sampled dogs were seropositive.

The probable role of dogs in the transmission of C. psittaci to human was suggested in a recent outbreak in Germany (Sprague et al., 2009). C. psittaci infection was reported in four bitches with recurrent kerato-conjunctivitis, severe respiratory distress, and reduced litter size (up to 50% stillborn or non-viable puppies) in a small dog-breeding facility in Germany (Sprague et al., 2009). Cell culture and immunofluorescence examination of conjunctival, nasal, and pharyngeal swabs revealed chlamydial inclusions. PCR and sequencing of ompA amplification products confirmed the presence of C. psittaci genotype C. The zoonotic potential of the pathogen was illustrated by evidence of disease in two children who lived on the premises with the infected dogs. There was circumstantial evidence to suggest infection

of dogs and humans may have followed the introduction of two canaries and a parrot into the household.

#### Corynebacterium ulcerans

Possible transmission of toxigenic Corynebacterium ulcerans from two dogs was suspected in a case of fatal diphtheria-like disease in an elderly woman in the United Kingdom (Hogg *et al.*, 2009). The woman had stayed on a 106-cow dairy farm shortly before becoming ill. Samples were collected on the farm (bulk tank milk and filter; milk samples from eight cows; and pharyngeal swabs from four dogs, two cats, and two guinea pigs). Toxigenic C. ulcerans was isolated from two of the farm dogs and the patient, and the two dogs had indistinguishable ribotype pattern.

#### Conclusions

Transmission of bacterial zoonoses from dogs to humans is rather uncommon. Transmission from dogs to humans occurs mainly through bites and by faecal shedding. Special attention should be given to young children who are more likely to be bitten by dogs or be in close contact with the pet and its environment. Respecting basic rules of hygiene, regular vaccination of dogs, removal of ectoparasites, and regular use of insecticides are important preventive measures that a dog owner should follow to prevent acquiring bacterial zoonoses from their pet.

#### Note

<sup>1</sup> www.cdc.gov.

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# **6** Dogs and Protozoan Zoonoses

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Protozoans are single-celled, eukaryotic organisms that often have complex life histories. Of the parasitic protozoans, only a small proportion is associated with disease and only a small percentage of these infects dogs. The few protozoans that infect dogs do not tend to be host-specific, but instead affect a variety of mammalian species. Notable among protozoans that infect both dogs and humans are Leishmania spp. which cause leishmaniasis, Trypanosoma cruzi which causes Chagas disease, and Giardia intestinalis which causes giardiasis. This chapter will focus primarily on these three conditions. Other protozoans that can infect both dogs and humans include Balantidium coli, Blastocystis hominis, Cryptosporidium spp., Cyclospora cayetanensis, Encephalitozoon cuniculi, Entamoeba histolytica, and Pentatrichomonas hominis. These protozoans will be discussed in less detail (Table 6.1).

## Leishmaniasis caused by *Leishmania* spp.

Leishmaniasis is predominantly a vector-borne disease caused by infection with the protozoan parasites *Leishmania* spp. There are numerous species and subspecies known to be pathogenic to mammals. The most common pathogenic species are often divided into New World species and Old World species based on geographic location, vector, and presenting clinical manifestations in infected humans (Box 6.1).

Of these pathogenic species, *L. chagasi/L. infantum, L. tropica, L. major,* and *L. braziliensis* are known to cause disease in both dogs and humans. In the New World (the western hemisphere), leishmaniasis is found in parts of the southern United States, Mexico, Central America, and South America. In the Old World (the eastern hemisphere), leishmaniasis is found in parts of Asia, the Middle East, Africa, and southern Europe.

## Leishmania spp. transmission

*Leishmania* spp. are most commonly transmitted by sandflies (sub-family Phlebotominae), with transmission linked to the geographic distribution of competent vectors. Reservoir hosts vary with *Leishmania* species and geographic location and can include a variety of wildlife species, dogs, and humans. Dogs are considered the most important peridomestic reservoir of *L. infantum* infection to humans. However, the extent to which

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Organism	Clinical signs in dogs	Clinical signs in humans	Route of transmission	Zoonotic potential	Reference
Balantidium coli	Asymptomatic; bloody diarrhoea	Diarrhoea (usually in immune-compromised individuals)	Faecal–oral, ingestion of cysts	Low	Barr, 2009b
Blastocystis hominis	Asymptomatic	Asymptomatic; diarrhoea	Undetermined; probably ingestion of cyst-like stage	Low	Greene, 2009
Cryptosporidium spp.	Asymptomatic; diarrhoea	Diarrhoea, nausea, vomiting, abdominal pain	Faecal–oral, ingestion of oocysts	Low	Lucio-Forster <i>et al</i> ., 2010
Cyclospora cayetanensis	Little clinical significance	Diarrhoea, nausea, low-grade fever, fatigue	Faecal–oral, ingestion of oocysts	Low	Ortega and Sanchez, 2010
Encephalitozoon cuniculi	Asymptomatic; encephalitis, nephritis	Multi-organ systemic disease in immune-compromised individuals	Faecal–oral, ingestion of spores; transplacental	Low	Snowden <i>et al.,</i> 2009
Entamoeba histolytica	Asymptomatic; mild to severe, ulcerative, haemorrhagic colitis	Diarrhoea with blood and mucus; liver abscesses	Faecal-oral	Low	Barr, 2009b
Pentatrichomonas hominis	Asymptomatic; commensal gut flora	Asymptomatic; commensal gut flora	Faecal–oral; no cyst stage; motile trophozoites possibly misdiagnosed as <i>Giardia</i>	Low	Bowman, 2007

## Table 6.1. Other zoonotic protozoans associated with dogs.

Box 6.1. New and Old World species of Leishmania spp.

#### New World species

L. braziliensis complex (L. braziliensis, L. panamensis, L. guyanensis)

L. mexicana complex (L. mexicana, L. amazonensis, L. venezuelensis)

L. peruviana

\*L. chagasi

#### Old World species

L. tropica complex (L. tropica, L. major, L. aethiopica) L. donovani \*L. infantum

\*It is now believed that L. chagasi and L. infantum are actually the same species.

dog ownership is a risk factor for human leishmaniasis is still unknown (Gavgani *et al.*, 2002). Cats and other domestic species are rarely infected, with the course of the disease often more limited in these species (Trainor *et al.*, 2010).

Leishmaniasis is typically transmitted by the bite of infected female sandflies. The sandflies inject the infective stage (promastigotes) during blood meals. Promastigotes are phagocytized by macrophages and other types of mononuclear phagocytic cells in the host. Promastigotes transform in these cells into the tissue stage of the parasite (amastigotes), which multiply by simple division and infect other mononuclear phagocytic cells. Sandflies then become infected by ingesting infected cells during blood meals. In sandflies, amastigotes transform into promastigotes, develop and multiply in the gut, and migrate to the proboscis where they are now ready to infect a new host. While transmission to both humans and other mammals usually occurs via a sandfly vector, in rare cases transplacental, venereal, and direct horizontal transmission between dogs has been documented. One of the most prominent examples of horizontal and vertical transmission is L. infantum transmission among foxhound populations located in North America (Boggiatto et al., 2011; Duprey et al., 2006).

#### **Disease in humans**

In humans, leishmaniasis manifests as either a cutaneous or visceral disease dependent on the leishmanial species, geographic location, and immune response of the host. According to the World Health Organization (WHO), an estimated 2 million new cases (1.5 million cases of cutaneous leishmaniasis and 500,000 cases of visceral leishmaniasis) occur annually, with about 12 million people currently infected worldwide (WHO, 2011).

The cutaneous form of the disease is characterized by one or more skin lesions on areas where sandflies have fed. The sores can change in size and appearance over time and often resemble a volcano, with a raised edge and a central crater. The sores can be painless or painful, with some individuals having swollen regional lymph nodes. Mucocutaneous leishmaniasis is a rare form of the disease that can occur months or years after the healing of a cutaneous leishmaniasis ulcer. This form can affect the nasal septum, palate, and other parts of the nasopharynx. The cutaneous form is most frequently caused by L. major and L. tropica in the Old World, and L. braziliensis, L. mexicana, and related species in the New World. According to the US Centers for Disease Control and Prevention (CDC), 90% of cutaneous leishmaniasis cases occur in parts of Afghanistan, Algeria, Iran, Saudi Arabia, Syria, Brazil, Colombia, Peru, and Bolivia.<sup>1</sup>

The visceral form of the disease often manifests as fever and weight loss accompanied by an enlarged spleen and liver. The disease can also result in a decrease in the production of blood cells that can lead to anaemia, bleeding, and opportunistic microbial infections. Without treatment, this form of the disease is nearly always fatal. Visceral leishmaniasis is becoming an important opportunistic infection in areas where it coexists with HIV (Nascimento *et al.*, 2011). According to the CDC, 90% of visceral leishmaniasis cases occur in parts of India, Bangladesh, Nepal, Sudan, Ethiopia, and Brazil.

#### Disease in dogs

Canine leishmaniasis typically has clinical signs similar to both cutaneous and visceral disease in humans. Cutaneous clinical manifestations include skin lesions, alopecia, and ulcerative or exfoliative dermatitis. Visceral lesions include swollen lymph nodes, progressive weight loss, epistaxis, and renal failure. Ocular signs (for example, blepharitis, conjunctivitis, keratitis, and anterior uveitis) have also been reported in dogs with leishmaniasis. Several possible predisposing factors to development of clinical signs, including breed and age, have been described (Sideris et al., 1999; Franca-Silva et al., 2003; Abranches et al., 1991; Cardoso et al., 2004). Subclinical infection is common among dogs living in endemic regions (Baneth et al., 2008).

#### Diagnosis and treatment

Leishmaniasis is definitively diagnosed by identifying Leishmania organisms in tissue biopsies, scrapings, or impression preparations by microscopy and/or culture in a specialized medium. Speciation is available through PCR methods. Serological tests such as the indirect fluorescent antibody test, direct agglutination, ELISA, or immunoblotting can also be helpful in achieving a diagnosis. The availability of these tests from commercial or fee-for-service laboratories varies depending on geographic location, with limited options in the United States. Antimonial drugs continue to be the best line of treatment for both affected humans and dogs (Oliva et al., 2010). However, complete clearance of the Leishmania organisms is rarely achieved in dogs, with relapse of the disease common. In contrast to visceral disease, cutaneous lesions in humans may heal independently of treatment. Clearance of lesions independent of therapy is not well documented in the dog.

At least one staging system, for dogs, has been devised to assist clinicians in determining the most appropriate therapy, as well as forecasting prognosis (Solano-Gallego *et al.*, 2011).

#### Prevention and control

The primary means of control of Leishmania spp. transmission is protection against sandfly bites. This includes avoiding outdoor activities, especially from dusk to dawn, when sandflies are generally most active. If one has to be outside during these times, wearing long-sleeved shirts and long trousers, and using insect repellent, help to decrease the chance of being bitten. In addition, sleeping in well-screened or air-conditioned houses will help to prevent the possibility of being bitten during the night. Alternatively, a bed net (preferably one treated with an insecticide) can be used. Elimination of seropositive dogs has been considered as a means to decrease human disease in endemic areas. However, studies from Brazil have shown no decrease in human cases after this control method was implemented (Nunes et al., 2008).

In dogs, use of insecticide-impregnated collars and topical spot-on formulations have been shown to be effective in reducing disease transmission in endemic areas (Alexander and Maroli, 2003; Maroli *et al.*, 2001; Miro *et al.*, 2007; Otranto *et al.*, 2007). A commercial vaccine against canine leishmaniasis has been approved for use in Brazil, and several vaccine candidates are under evaluation in Europe (Borja-Cabrera *et al.*, 2002; Dantas-Torres, 2006; Lemesre *et al.*, 2007; Ramos *et al.*, 2008).

## Zoonotic potential and public health considerations

Leishmaniasis continues to be considered a public health threat throughout much of the developing world, with transmission of *L. infantum* from dogs or wildlife reservoirs via sand flies an important route for human infection. Several studies have reported that increased prevalence of *L. infantum* in canine populations is associated with increased incidence of human leishmaniasis (Margonari *et al.*, 2006; Werneck *et al.*, 2007). In addition, low socio-economic status, dog density, and ownership of an infected dog have been shown to be risk factors for human disease (Acedo Sánchez *et al.*, 1996; Gavgani *et al.*, 2002; Werneck *et al.*, 2007).

## Chagas Disease caused by Trypanosoma cruzi

Chagas disease, also called American trypanosomiasis, is a vector-borne disease caused by infection with the protozoan parasite Trypanosoma cruzi. A wide range of mammalian species including dogs, humans, and wildlife (opossum, raccoon, armadillo, and a variety of rodents) have been documented as hosts for the parasite (John and Hoppe, 1986; Karsten et al., 1992; Yabsley and Noblet, 2002). This parasite is restricted to the western hemisphere based on the geographic distribution of the arthropod vector commonly known as 'kissing bugs' or 'cone-nosed bugs' (Hemiptera: Reduviidae). The highest human infection rates have been reported in parts of South America, particularly Argentina, Bolivia, Brazil, and Columbia, but human Chagas disease has also been documented in Central American countries and Mexico (Estrada-Franco et al., 2006; WHO, 2010). T. cruzi has also been identified in sylvatic reservoir hosts and dogs in the southern United States extending from Maryland and the Carolinas through Oklahoma, Texas and Louisiana, and rare human cases have also been reported in the United States (Dorn et al., 2007; Herwalt et al., 2000; Karsten et al., 1992; Kjos et al., 2008, 2009a; Walton et al., 1958; Yabsley and Noblet, 2002).

#### Transmission

*T. cruzi* transmission is typically based on a stercorarian mechanism where the parasite localizes in the hindgut of the triatomine bug vector. The extracellular flagellated epimastigote form of the parasite multiplies in

the bug hindgut. The infective parasites are passed in the bug faeces at the time of feeding to contaminate the bite wound, skin lesions, or mucous membranes of the mammalian host. The extracellular trypomastigote form is found briefly in peripheral blood of the mammalian host, and the more persistent intracellular amastigote form multiplies intracellularly in the skeletal muscle, lymph nodes, and other tissues. The life cycle is completed when the triatomine bug ingests parasites while feeding on the infected mammalian host.

Members of the Triatominae bug subfamily (Hemiptera: Reduviidae) are obligate blood feeders in all post-egg stages, and are biological arthropod vectors for the parasite. Triatomine bugs utilize a broad range of vertebrate hosts including mammals, birds, and reptiles, but only mammals are susceptible to infection with T. cruzi. Ten of the 11 bug species found in the United States are competent vectors of T. cruzi, including nine members of the genus Triatoma (T. gerstaeckeri, T. indictiva, T. lecticularia, T. neotoma, T. protracta, T. recurva, T. rubida, T. rubrofasciata, and T. sanguisuga) and Paratriatoma hirsuta (Kjos et al., 2009a). In Latin America, bugs in the Panstrongylus and Rodnius genera are also important vectors. Although all triatomine species are considered potential disease vectors, only species that have adapted to living in or near domestic structures are of primary public health importance. The usual transmission of Trypanosoma cruzi in endemic countries depends on the confluence of reservoirs, vectors, parasites, and hosts (people or animals) in a single habitat.

Although the stercorarian route is regarded as the major route of parasite transmission, oral transmission of *T. cruzi* has also been documented in dogs, opossums, raccoons, and wood rats after they ingest infected bugs (Roelling *et al.*, 2009). Similarly, oral transmission of the parasite has been documented in humans after consumption of unpasteurized fruit juice containing infected bug parts (Pereira *et al.*, 2009). Less commonly, transplacental transmission of parasites has been documented in humans and dogs (Pereira *et al.*, 2009; Kjos *et al.*, 2008). Blood transfusion has been identified as another
possible route of transmission in humans. The US Food and Drug Administration (FDA) approved a diagnostic blood screening test in 2007 for voluntary use, so many blood bank systems in the United States have joined other countries by routinely screen blood products.<sup>2</sup> Cases of parasite transmission through organ transplantation have also been documented in Latin America and rarely in the United States (Casadei, 2010).

#### Disease in humans

An estimated 10 million people are infected with *T. cruzi*, mostly in Latin America, and the WHO categorizes Chagas disease as one of the neglected tropical diseases (WHO, 2010). Based on seroprevalence studies in immigrant populations, the CDC estimates that more than 300,000 people who acquired their infections in endemic countries now live in the USA.<sup>3</sup>

The clinical disease caused by *T. cruzi* is generally described in two phases, and infection is lifelong if untreated (Pereira *et al.*, 2009; WHO, 2010). In the initial acute phase, which can last up to 2 months, a high number of trypomastigotes may be detected in circulation. Often people are asymptomatic, and clinical signs may be mild to severe with fever, headache, enlarged lymph nodes, muscle pain, and sometimes swelling at the inoculation site.

The acute phase is typically followed by a prolonged 'indeterminate' stage where people are asymptomatic and often unaware of their infection. This stage can persist for years, and some people never develop chronic Chagasrelated symptoms. In the chronic, progressive stage of the disease, the target tissues for amastigote replication and organ dysfunction include the heart and digestive system smooth muscle and innervating ganglia. Up to 30% of chronically infected people develop cardiac disease that results in acute death or endstage heart failure. Reported cardiac disorders include arrhythmias and other electrical conduction disturbances, and cardiac muscle damage resulting in chronic progressive dilatative cardiomyopathy. Digestive disorders caused by megaoesophagus and/or megacolon develop in about 10% of chronically infected

people. A combination of cardiac and digestive organ damage often occurs.

#### **Disease in dogs**

Acute and chronic cases of Chagas disease have been reported in domestic dogs in the United States and many Latin American countries. The pattern of infection in dogs appears to follow the cardiac disease pattern in humans, while megaoesophagus and other megaviscus syndromes described in humans have not been reported in dogs (Barr, 2009a; Snowden and Kjos, 2012). Acute disease is sudden in onset, with signs of myocarditis and cardiac arrhythmias. In one report reviewing the histopathologic records of 86 canine Chagas cases, 42% of the previously normal animals were reported as acute deaths, and most were young dogs (Kjos et al., 2008). Survivors of acute myocarditis become aparasitaemic and asymptomatic in the indeterminate or latent phase. Although not all dogs progress to chronic disease, many develop bilateral cardiac dilatation over a variable length of time. One sometimes overlooked aspect of chronic infection is electrical conduction disturbance with variable cardiomegaly, reported in 21% of the cases in a recent report (Kjos et al., 2008). Abnormalities include atrial fibrillation, ventricular premature contractions, first and second degree heart block and tachyarrhythmias, and a number of animals are candidates for pacemaker implantation (Barr, 2009a; Kjos et al., 2008).

#### **Diagnosis and treatment**

In both humans and dogs, a definitive diagnosis is usually made based on a combination of appropriate (geographic) history of possible exposure, and clinical signs/ symptoms supported by microscopic identification of parasites on blood films and/or positive serologic testing. In the acute phase, trypomastigotes are identified on stained blood films when parasitaemias are high, but organisms are difficult to identify microscopically during chronic stages of infection. To detect parasite specific antibodies during chronic infection, a selection of serologic tests are available in a variety of test formats such as ELISA, immunofluorescent, or immunochromatic tests (Nieto et al., 2009). These tests are variably available for humans or for dogs depending on geographic location (United States versus Latin American countries). One important concern to note is the serologic cross reactivity between T. cruzi and visceral Leishmania parasites in both dogs and humans (Duprey et al., 2006). The specificity of different serologic tests varies, and the possibility of misdiagnosis exists in geographic regions where both parasites are endemic.

Radiographic or ultrasononographic evidence of cardiac enlargement or electrocardiographic evidence of conduction abnormalities also support a diagnosis of Chagas disease (Barr *et al.*, 1992). Less commonly, xenodiagnosis (examination of triatomine bugs fed with the patient's blood), haemoculture, or molecular methods are used on a research basis. Post-mortem identification of parasites in histologic sections of cardiac muscle or digestive organs provides a definitive diagnosis (Snowden and Kjos, 2012).

Success of treatment in humans depends largely on rapid diagnosis and initiation of treatment early in the acute phase. In Latin America, acute Chagas disease in humans can often be successfully treated with the drugs nifurtimox or benznidazole (WHO, 2010). Treatment of chronic disease is much less rewarding, and the value of treatment with either of these drugs is debated. Unfortunately, neither of these drugs is available in the United States. Supportive treatments for cardiac or digestive manifestations are often helpful in improving the quality of life of chronically infected individuals.

Therapeutic options for treating *T. cruzi* infections in dogs are limited. In Latin America, treatment of humans rather than dogs is a primary focus; and in the United States, appropriate drugs are not available. In limited research studies, nifurtimox showed some success in treating experimental and natural cases of canine trypanosomiasis, but severe side effects limited its use (Haberkorn and Gonnert, 1972). The second drug approved for

human use, benznidazole, also showed some success in treating acute infections, but had less efficacy in treating chronic cases in experimentally infected dogs (Guedes *et al.*, 2002).

#### Prevention and control

In Latin America, prevention of Chagas disease in humans has primarily focused on reduction of domiciliated bug vectors through the use of appropriate pesticide regimens. Additionally, screening of the blood supply has reduced the risk of transfusion-associated infection. Similar triatomine bug control mechanisms could be employed in the United States to reduce T. cruzi infection among domestic dogs. Currently there are no pesticides in the United States specifically labelled for control of triatomine bugs. However, residual spray formulations of synthetic pyrethroids, such as deltamethrin, have proved to be very effective at killing the Chagas disease vectors in Latin America, and are available in the United States (Rojas de Arias et al., 2003).

In addition to the use of appropriate pesticides, control measures could include housing dogs indoors at night if possible, using mechanical barriers around indoor kennels to minimize bug entry into premises (e.g. plugging drains or other openings and securing movable doors), and limiting the use of yard lights to reduce attraction of insects (Snowden and Kjos, 2012).

Removing serologically positive breeding stock from kennels may reduce the risk of dog–bug–dog transmission. Additionally, the risk of transplacental transmission of the parasite will be virtually eliminated if only serologically negative bitches are used for breeding purposes.

# Zoonotic potential and public health considerations

Chagas disease continues to pose a significant health threat in the Americas. Domestic dogs in South America play a significant role as competent parasite reservoirs and blood hosts for the triatomine vectors, and serve as surveillance sentinels for domestic transmission. Studies in endemic areas of Argentina have shown that dogs have a high capacity to infect triatomine bugs due to persistent parasitaemia (Gürtler et al., 2007). The importance of dogs as Chagas disease reservoirs in the United States has not been determined but probably depends on host characteristics, bug vector feeding behaviour, and parasite strain virulence. Seropositive dogs were identified in close proximity to two autochthonous US human cases, providing some evidence of canine involvement in vectorborne transmission in this region (Herwaldt et al., 2000; Navin et al., 1985). In a survey of triatomine bugs collected from peridomestic settings in Texas, DNA-based blood meal analysis revealed that Triatoma gerstaeckeri and *T. sanguisuga* utilize dogs as blood hosts (Kjos et al., 2009b). Additional research is required to fully understand the role of dogs in the Chagas disease transmission cycle in the United States.

Although human Chagas disease in the United States is almost certainly under-recognized due to a predominance of mild and/or latent manifestations and low awareness among physicians, vector-borne human transmission is significantly lower than in Latin American countries. In the United States, the low probability of human contact with infected triatomine species is probably the major reason for the low transmission rates (Kjos *et al.*, 2009b). However, the same low level transmission is not reflected in the domestic dog population. The disparity in prevalence between dogs and humans in the United States may be due to differences in vector exposure levels and transmission routes. Oral ingestion of infected triatomine bugs may be a significant route of infection for dogs. Dogs housed in outdoor kennels have more opportunity for encounters with triatomine bugs than humans, or animals that sleep inside houses at night. Hunting dogs, which tend to experience the highest Chagas disease prevalence rates in the United States, are typically housed in outdoor kennels. Regardless of the mechanism, exposure to infected vectors appears to play a role in canine Chagas disease in the United States, as supported by reports of infected bug specimens

found in close proximity to cases (Beard *et al.,* 2003; Kjos *et al.,* 2009a).

# Giardiasis caused by Giardia intestinalis (syn. G. duodenalis, G. lamblia)

Giardia intestinalis is a flagellated extracellular protozoan pathogen that localizes in the small intestine of a wide range of mammalian hosts including dogs and humans. The parasite is global in distribution, and is recognized as one of the most common enteric parasites of domestic animals and humans (Thompson *et al.*, 2008). The scientific names identifying this organism include G. lamblia and G. duodenalis as well as G. intestinalis. Depending on the date of publication and author preferences, all three of these names can be commonly found in scientific literature and are assumed to be synonymous. Giardiasis is caused by Giardia intestinalis (syn. G. duodenalis, G. lamblia).

The parasite is common in dogs and cats, with several recent surveys reporting a wide range of prevalence values depending on the pet population surveyed, the host species, the diagnostic method used to detect the organism, and other factors which may bias such types of surveys. In a US study using a commercially available faecal antigen detection test on faecal samples from symptomatic animals, 15.6% of more than 16,000 dogs and 10.8% of almost 5000 cats were positive for the parasite (Carlin et al., 2006). In a similar European study using the same diagnostic test for symptomatic animals, 24.8% of 8685 dogs and 20.3% of 4214 cats were positive (Epe et al., 2010). In a cross-sectional study in England using the same diagnostic test, 9.9% of 878 dogs were positive, indicating a much lower prevalence in a general population of animals (Upjohn et al., 2010). In another US national survey using zinc sulphate centrifugal flotation of approximately 1.2 million canine samples (no clinical histories available), 4% were positive, with an age-related decreasing prevalence ranging from 13.1% in dogs less than 6 months of age to 1.5% in dogs over 7 years of age (Little et al., 2009).

The prevalence of Giardia infections in humans is also difficult to determine due to a lack of standardized test methods and reporting systems. In the United States, the CDC reported over 19,000 human cases annually for the years 2006, 2007, and 2008, based largely on voluntary data collected by the National Notifiable Disease Surveillance System (Yoder et al., 2010). Incidence of giardiasis cases per 100,000 population ranged from 2.2 to 33.8 cases at the state level in 2008. Surveillance data also showed the highest case numbers in children aged 1-4 followed by children aged 5-9. It is assumed that these data underestimate the giardiasis burden in humans in the United States because the infection can be asymptomatic, not all infected persons seek medical care, appropriate laboratory diagnostics are not always completed, and data are under-reported (Yoder et al., 2010).

In a recent review summarizing prevalence data from a number of human studies from 20 European countries, prevalence ranged from approximately 1% to 11% in asymptomatic people, and from approximately 2% to 18% in symptomatic cases, with the highest values reported in children (Plutzer *et al.*, 2010). In a recent review summarizing published data from 28 human studies across Asia, prevalence ranged from 1% to 73% (Dib et al., 2008). Data from these and other epidemiologic studies confirm that Giardia is a common parasite in both humans and dogs in widespread geographic locations. Data from both human and pet studies show agreement in the age-related trend for higher infection rates in children and young animals.

*Giardia* infections have been documented in a number of additional domestic animals including goats, sheep, cattle, swine, and horses, as well as in wildlife such as nutria, muskrat, beaver, otter, and aquatic birds (reviewed in Plutzer *et al.*, 2010). The role of these animals as reservoirs of infection that cause environmental contamination with infective cysts has been widely debated.

#### Transmission

The *Giardia* organism has a direct life cycle with two morphologic forms. The trophozoite

is the motile, metabolically active, tear-drop shaped, flagellated form that replicates at the villous epithelial surface of the small intestine. As organisms move caudally in the gastrointestinal tract with ingesta, they transform to the oval, non-motile, non-reproducing cyst stage that is passed in the faeces. Cysts are immediately infective when ingested by the appropriate mammalian host (Thompson et al., 2008). Potential mechanisms of transfer include person to person, animal to animal, or zoonotic (animal to human or human to animal), usually in an indirect manner through environmental contamination (Plutzer et al., 2010). The cysts are environmentally resistant and can survive for months in soil or surface water in temperate conditions (Plutzer et al., 2010). In human experimental studies, an infective dose of as few as 10-100 cysts were needed to establish an infection and cause diarrhoea (Ballweber et al., 2010). In experimental canine infections, the onset of cyst shedding has been reported to be as short as 5-7 days after cyst ingestion (Ballweber et al., 2010). An infected person or animal can shed variable numbers of cysts intermittently in their faeces, and the duration of shedding can last for weeks to several months (Yoder et al., 2010).

Beyond the generalized faecal-oral transmission pattern, data are not generally available regarding individual animal to animal transmission mechanisms, and animal outbreaks are not well documented. Transmission patterns are better studied in humans, where transmission of the parasite is frequently associated with cyst-contaminated water. Outbreaks are frequently linked to contaminated communal water sources such as swimming pools, lakes, and rivers. A seasonal peak in case reports coincides with summer recreational water usage, especially in children in the United States (Yoder et al., 2010). Additionally, over a 10-year period, Giardia was the cause of 15 of 141 (10.6%) reported drinking-water-associated gastroenteritis outbreaks in the United States (Yoder et al., 2010). Foodborne transmission of Giardia is less frequent, and is usually associated with direct contamination of food by an infected food handler, or by using contaminated water in food preparation.

## Disease in humans and dogs

The clinical disease in humans and dogs is generally similar. This enteric pathogen causes a spectrum of clinical manifestations ranging from asymptomatic, to acute, intermittent, or chronic diarrhoea. Typically the disease is characterized by non-bloody soft formed to unformed faeces, abdominal cramps, anorexia, bloating, and malabsorption; and sometimes nausea, vomiting, and steatorrhoea with or without weight loss (Ballweber *et al.*, 2010; Yoder *et al.*, 2010).

The reasons for the spectrum of clinical disease are unclear, but they are probably due to a number of interacting host and parasite factors. The Giardia trophozoites are not invasive and do not cause significant morphologic injury to the small intestinal mucosa. A number of pathophysiologic mechanisms are being explored as a cause of the diarrhoea that commonly is associated with this parasite infection. In a variety of research reports, a number of mechanisms have been suggested including increased enterocyte apoptosis, loss of intestinal epithelial barrier function causing increased permeability, and abnormal transport of electrolyte and nutrients at the epithelial microvillous border (reviewed by Buret, 2008). A number of concurrent gastrointestinal conditions such as a disruption of commensal microbial gut flora, food allergies, or the presence of additional microbial enteropathogens have also been suggested as influential factors in the onset, duration, and severity of clinical disease.

The development of protective immunity against *Giardia* has not been clearly proven in human or domestic animal hosts. It is unclear whether intermittent diarrhoea episodes are an indication of continued infection despite treatment, or whether reinfection occurs readily, causing repeated clinical occurrences of disease.

#### Diagnosis

A variety of microscopic and immunodiagnostic tests that detect *Giardia* cysts in faeces are available either as in-house or diagnostic laboratory fee-for-service assays. Parasitologic methods using faecal flotation and microscopy are widely used in veterinary clinics. Variations on those methods including a centrifugal flotation technique, particularly using zinc sulphate flotation solution (specific gravity 1.18) and formol-ethyl sedimentation have been described (Mekaru et al., 2007; Zajac and Conboy, 2006). The sensitivity and specificity of these methods vary depending on the specific protocol and the skill of the microscopist. Stained faecal smears made from fixed faecal samples are sometimes evaluated in human laboratories, but generally lack sensitivity (Ballweber et al., 2010). Wet mounts of fresh liquid faeces may sometimes show motile trophozoites; however, this method lacks sensitivity. Rapid evaluation of fresh samples is essential since the trophozoites are not environmentally stable and rapidly lose their motility under cool or drying conditions. The light microscopic methods are typically rapid and inexpensive to perform.

direct immunofluorescent assay А (Merifluor Cryptosporidium/Giardia assay, Meridian Bioscience) is often considered the 'gold standard' method in both human and veterinary diagnostic laboratories because of excellent specificity and good sensitivity of this method (Ballweber et al., 2010; Mekaru et al., 2007; Plutzer et al., 2010; Rishniw et al., 2010; Yoder et al., 2010). This technique has limited usage in veterinary clinics or many hospital laboratories because of the need for a compound microscope with appropriate UV light source and barrier filters to complete the assay, but it is a commonly used assay in veterinary diagnostic laboratories and commercial fee-for-service laboratories.

A number of faecal antigen detection immunodiagnostic tests in single or multi-well ELISA or card formats are commercially available for both human and veterinary use. Sometimes assays designed for human use are utilized for companion animal sample testing, with variable results (Mekaru *et al.*, 2007). Additionally, a point-of-use lateral flow faecal antigen detection test (Giardia SNAP test, IDEXX Laboratories) is frequently used in veterinary practices for evaluating individual patient samples, as well as in epidemiological surveys in the United States and Europe (Carlin et al., 2006; Epe et al., 2010; Upjohn et al., 2010). Disappointingly, there is often a discrepancy in analysing a single sample using multiple methods with either domestic animal or human samples (Mekaru et al., 2007; Rishniw et al., 2010; Vidal and Catapani 2005). It is generally reported that the immunodiagnostic tests detect a higher number of positive samples than microscopy, at a greater cost/test (Vidal and Catapani, 2005). Using a combination of immunodiagnostic and parasitologic microscopy methods ensures the most accurate diagnosis of this parasite. The use of multiple samples collected over several days also increases the sensitivity of detection of Giardia (Vidal and Catapani, 2005; Zajac and Conboy, 2006).

Additionally, molecular methods are being developed to identify the parasite, often as part of a multi-pathogen PCR assay or real-time PCR assay (Amar *et al.*, 2007; de Boer *et al.*, 2010). Many research reports describe the development of these molecular methods using both human and animal faecal samples. The availability of molecular diagnostic tests on a feefor-service basis from a commercial diagnostic laboratory varies, depending on the geographic location, but this diagnostic option is expanding in both medical and veterinary laboratories.

In outbreak investigations, it is often helpful to evaluate environmental samples as possible sources of cysts. Standardized protocols using fluorescent microscopy and/ or molecular methods are now available for processing both water and soil samples to concentrate and detect *Giardia* cysts in the environment (Thompson *et al.*, 2008).

#### Treatment

A variety of drugs has been used to treat giardiasis in domestic animals and humans. In humans, the oral anti-protozoal drug, metronidazole, is widely used as a multi-dose treatment against giardiasis. However, that compound is not approved for animal use and is prescribed by veterinarians in the United States under the Animal Medicinal Drug Use Clarification Act. A number of detrimental side effects have been reported, and the efficacy of the product is variable, suggesting that parasite resistance may occur (Montoya *et al.*, 2008; Thompson *et al.*, 2008).

Several compounds in the benzimidazole family have been widely used as treatment against giardiasis. The efficacy of fenbendazole, oxfendazole, and albendazole has been shown in either experimental canine infections or in clinical studies, using varied treatment dosage, frequency, and duration regimens (reviewed by Thompson et al., 2008). Animals treated with these compounds generally show clinical improvement and decreased parasite cyst shedding with a low rate of adverse reactions, although a 'cure' is not assured. Although specific formulations differ when comparing products from the United States and Europe, several combination products that include the closely related pro-benzimidazole compound, febantel, along with praziquantel and pyrantel, have shown good efficacy when used in a multi-day treatment regimen (Montoya et al., 2008; Thompson *et al.*, 2008).

Additional compounds such as furazolidone and quinacrine have been reported in older literature as treatments for giardiasis, but are not currently used widely as veterinary products labelled for dogs or cats in the United States (Thompson *et al.*, 2008).

As with any case of diarrhoea, the severity of dehydration and electrolyte imbalance should be determined on a recurrent basis in symptomatic human or animal patients. Fluid therapy should be administered as supportive treatment as appropriate.

As previously noted, asymptomatic shedding of *Giardia* cysts has been reported in both humans and dogs. One controversial point in veterinary medicine is whether to prescribe medication to a clinically normal animal with faecal shedding of cysts.

#### **Prevention and control**

Since infection occurs through the ingestion of infective cysts either directly or indirectly through faecal–oral contact, the practice of good hygiene is the key to minimize exposure to the parasite. The CDC has published a detailed list of recommendations to prevent and control giardiasis in humans, and these approaches can readily be applied to pets and their environments as appropriate (Yoder et al., 2010). Some of the most important points emphasize effective hand washing before eating, after using the toilet, after changing nappies or tending someone who is ill with diarrhoea, and after handling animal wastes. Other recommendations include avoiding potentially unclean water sources such as swimming pools, lakes, rivers, inadequately treated drinking water or ice, or uncooked foods that were prepared using contaminated water. Additionally, in human-pet interactions, the CDC recommends minimizing contact with the faecal materials of all animals, using gloves when cleaning up animal faeces, and washing hands after handling those faeces.

One additional control approach for dogs and cats that is no longer commercially available is a vaccine (GiardiaVax for Dogs<sup>®</sup> and GiardiaVax for Cats<sup>®</sup>, Ft Dodge Animal Health, Charles City, Iowa). Interestingly, the vaccine product label defined the efficacy of the vaccine as a decreased severity and duration of diarrhoea if the animal because ill, and a decreased number and duration of cyst shedding. It is unclear whether a similar vaccine will become commercially available in the future.

#### Zoonotic potential and public health considerations

The zoonotic potential of Giardia isolates has been experimentally demonstrated using parasites from both humans and animals (Plutzer et al., 2010). However, the relative importance of zoonotic transmission of the parasite is an area of continued study and debate. Based on molecular data, multilocus genetic sequence analyses, and comparisons of numerous isolates from a variety of hosts have resulted in the description of at least seven genetically distinct groups called genotypes or assemblages identified as 'A' to 'G' types (reviewed by Ballweber et al., 2010; Thompson et al., 2008). In additional groupings, subtypes AI to AIV have been identified within assemblage A. Generally, there is a consensus that humans are the predominant host for assemblage

A. Humans and dogs (or occasionally other mammals) have been infected with assemblage B, indicating this genotype clearly has zoonotic potential. Assemblages C and D are found in dogs, E is found in cattle and hoofed stock, F is found in cats, and G is described in rodents (reviewed by Ballweber *et al.*, 2010; Thompson *et al.*, 2008).

It is increasingly clear that molecular epidemiologic studies are having an enormous impact on Giardia at the species and intraspecific levels. Ballweber et al. (2010) summarized data from 36 studies that reported discrepant information regarding the relative distribution of the various assemblages among different hosts and their importance in transmission of the parasite from pets to humans. Based on several recent studies using these molecular technologies in taxonomic studies, it is now recognized that most isolates found in humans were probably transmitted indirectly from other humans, and that the zoonotic importance of parasite transmission is diminishing (Thompson et al., 2008). It is suggested that local environmental conditions, local parasite strain variation, and relative intensity of human-animal contact will influence the potential for zoonotic transmission of this parasite.

To clarify the genetic variations and transmissibility of parasite assemblages among different hosts, some scientists have proposed changes in nomenclature. *Giardia* assemblage A found mostly in humans remains *G. duodenalis*, while assemblage B would become the zoonotic *G. enterica* species. Based on a more restricted host preference, assemblages C, E, F, and G would become *G. canis* in dogs, *G. bovis* in hoofed stock, *G. cati* in cats, and *G. simondi* in rats, respectively. Whether this revised nomenclature is accepted in the scientific community remains to be seen.

#### Conclusions

While there are a number of protozoan organisms that infect both dogs and humans, most of these do not cause clinical disease, or only cause mild disease in dog and/or human hosts. The most notable exceptions are *Leishmania* spp., *Trypanosoma cruzi*, and *Giardia intestinalis*. These three conditions continue to cause public health problems on either a regional or global scale, with additional research needed to better elucidate the roles that dogs play in the transmission of these protozoan parasites to humans.

#### Notes

<sup>1</sup> www.cdc.gov/parasites/leishmaniasis, accessed 8 June 2012.

<sup>2</sup> www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/ BloodDonorScreening/InfectiousDisease/ucm126585.htm, accessed 7 June 2012.

<sup>3</sup> www.cdc.gov/parasites/chagas/epi.html, accessed 8 June 2012.

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# 7 Dogs and Trematode Zoonoses<sup>1</sup>

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The trematodes or flukes belong to the Phylum Platyhelminthes. They are all endoparasites and are characteristically flat and leaf-like, or occasionally globular, hermaphroditic organisms (except for one group, the schistosomes, which have a male folded about its long axis and a cylindrical female). Adults have a blindly ending bifurcate intestine without an anus and two suckers: an anterior oral sucker surrounding the mouth, and a more posterior ventral sucker or acetabulum by which the worm attaches itself to the host. All organs are surrounded by parenchyma as there is no coelom, and the outer tegument, which often contains spines, is composed of a syncytial cytoplasmic layer which secretes enzymes and is of great importance in nutrition; it is thus an antigenically active site.

Trematodes have an indirect life cycle which always involves a snail as first intermediate host. Most are freshwater species of snails but a few utilize terrestrial snails (e.g. *Dicrocoelium dendriticum*) or, for sea birds, marine species. Inside the snail all trematodes undergo asexual reproduction and most which parasitize both humans and dogs have a cystic stage in a secondary intermediate host such as a fish or edible crustacean (again except for the schistosomes, in which larvae penetrate the skin). Thus infection depends very much on the dietary habits of the hosts. Adult trematodes are very catholic in their choice of definitive host, although almost all are very specific in which snails they can develop. There are over 60 trematode species which have been reported from both humans and dogs (listed in Table 7.1), but for many trematodes they are occasional hosts only, and dogs are not the most important reservoir hosts of human infection.

The trematode parasites of dogs are considered in standard textbooks (Dunn, 1978; Euzeby, 1982; Georgi and Georgi, 1992; FAO, 1994; Kaufmann, 1996; Kassai, 1999; Schnieder, 2006; Bowman, 2009) and zoonotic trematode parasites in general in various monographs (Malek, 1980; Hillyer and Hopla, 1982; Schultz, 1982; Geerts *et al.*, 1987; Hugh-Jones *et al.*, 1995; WHO, 1995; Hinz, 1996; Muller, 2002; Cheesbrough, 2006; Crompton and Savioli, 2007).

## The Schistosomes

# Superfamily Schistosomatoidea: Family Schistosomatidae

Five species of schistosomes (*Schistosoma haematobium*, *S. intercalatum*, *S. japonicum*, *S. mansoni*, and *S. mekongi*) are the cause of schistosomiasis, which is prevalent in 57 countries

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across America, Africa, and Asia. In 2009, the estimated number of people infected was 239 million, while 765 million were living in areas where schistosomiasis is transmitted (population at-risk) (WHO, 2010). Schistosomiasis in humans is primarily a rural disease, particularly affecting children; adults are also at-risk, especially in agricultural and fishing communities.

Of the primarily human species, S. japonicum is a true zoonosis and dogs as well as bovines are often infected and act as reservoir hosts. Human infection is principally confined to China, Sulawesi, and the Philippines. In 2009 there were estimated to be 730,000 cases in China, 25,000 in Indonesia, and 576,000 in the Philippines (WHO, 2010). In China many animals can act as reservoir hosts but the most important are bovines (with up to 90% infection rates in cattle and buffalo) and dogs (10% infected) (Jordan et al., 1993). In spite of widespread and effective control achieved in recent years in China, the recent construction of the Three Gorges Dam on the Yangtze river is likely to represent a significant threat in terms of expansion of population at-risk (Zhu et al., 2008; McManus et al., 2010). In Taiwan, infection occurs only in animal hosts and humans are refractory (Fan, 2003).

*S. mekongi* is morphologically similar to *S. japonicum*, and is an important human parasite in the Mekong valley regions of Laos and Cambodia. After years of effective control, the number of people infected and at-risk has been reduced to 14,000 and 82,000 in Cambodia, and 31,000 and 112,000 in Laos, respectively (WHO, 2010). Dogs are the only reservoir hosts.

*S. mansoni* is widely distributed in Africa and also occurs in foci in the Middle East, South America, and the Caribbean (principally Puerto Rico and the Dominican Republic). Reservoir hosts are of little epidemiological significance although primates and rodents may be of local importance. Dogs can be infected but often do not pass eggs (Jordan *et al.*, 1993).

*S. haematobium* is the most widespread species globally, while *S. intercalatum* is only transmitted in isolated foci in central Africa; neither is a zoonosis and so they are not considered here.

Adult S. japonicum, S. mansoni, and S. mekongi worms live in the posterior mesenteric veins, the smaller and thinner female residing permanently in a canal formed by the fleshy ventral folds of the male which measures about 12 mm. Eggs (those of S. japonicum and *S. mekongi* measuring  $85 \times 60 \,\mu$ m with a small knob, and those of *S. mansoni* measuring 140 ×  $60\,\mu\text{m}$  and with a lateral spine) are laid in the small venules, penetrate through the wall of the large intestine, and are passed out in faeces. On reaching freshwater a larva, known as a miracidium, emerges and penetrates into a suitable species of snail (see Table 7.1), multiplies inside the snail; a few weeks later the next free-living, fork-tailed larval stage, the cercaria, emerges and can survive for a few days in water. If it comes into contact with a susceptible mammal it penetrates through the skin by means of histolytic glands, reaches the lungs, and then migrates to its final site via the pulmonary veins.

The adult worms do little damage, but in chronic infections more and more eggs become trapped in the tissues, producing an inflammatory response, leading to the formation of granulomas and eventually extensive fibrosis. This phase of infection may be symptomless or accompanied by bloody intermittent diarrhoea and headache. However, in heavy infections eggs get carried through the portal venous system to the liver, and granulomas formed around them there lead in 5-15 years to extensive fibrosis surrounding the branches of the portal vein. This causes portal hypertension with enlargement of the liver and spleen, and compensatory enlargement of the minor veins from the liver which can burst, causing death (Rollinson and Simpson, 1987; Guttierez, 1990; Jordan et al., 1993). Diagnosis is by finding eggs in the faeces or by serological methods such as ELISA, which detect antibodies or circulating antigens released by worms in the bloodstream; detection of antigens on urine or faecal samples is also possible by immunological or molecular methods. Effective treatment is possible with praziguantel for all species, or with oxamniquine for S. mansoni only.

The epidemiology of schistosomiasis is determined by the habits of the snail intermediate hosts. Those of *S. japonicum* live either in the muddy margins of streams and rivers (in China) or in rice paddies (in the Philippines), while the natural habit of snails transmitting S. mekongi is constituted by the small crevices in partially submerged rocks and stones on the river bed. Snails of S. mansoni inhabit slow-flowing streams, irrigation canals, or large ponds or lakes. The distribution of S. mansoni is increasing in Africa because of many new irrigation schemes, particularly the large-scale ones in Egypt and Sudan. Prevention is by avoiding contact with water in which transmission may be occurring. Possible control measures include health education; environmental management; sanitation; snail control; and, especially, preventive chemotherapy - the regular, large-scale distribution of praziguantel to individuals at-risk (Savioli et al., 1997; WHO, 2002, Crompton and Savioli, 2007; WHO, 2006).

Heterobilharzia americana is a trematode related to Schistosoma spp. and is the causal agent of canine schistosomiasis. It is a parasite of dogs and other mammals in the south-western United States (Johnson, 2010). In humans the penetrating cercariae cannot develop further and cause a dermatitis, similar to that caused by many bird schistosomes and known as 'swimmer's itch'. Dogs get infected by paddling in swampy areas or swimming in canals in areas where raccoons, the natural reservoir of the infection, are present. Symptoms and signs in dogs include lethargy, loss of weight, anorexia, vomiting, chronic intermittent dysentery, and inflammation of the lymph nodes (lymphadenopathy); anaemia and hypercalcaemia are frequent (Fabrick et al., 2010). Praziquantel and fenbendazole are effective treatments.

# The Opisthorchids

# Superfamily Opisthorchioidea: Family Opisthorchiidae

Members of this family are typically flattened, elongate, hermaphroditic flukes, measuring 5–20mm in length. The adults are found in the hepatic and pancreatic ducts of fish-eating mammals (including humans) or birds, and the cercariae encyst in freshwater fish (Table 7.1).

It is estimated that 7-19 million people are infected with Clonorchis sinensis worldwide, while at least 8 million are infected with Opisthorchis viverrini and 0.4-1.5 million are infected with O. felineus (WHO, 1995; Fürst, 2012; Haswell-Elkins and Elkins, 1998; Muller, 2002). Both genera are very similar in morphology and life cycle, the main difference being that in Clonorchis the testes are in tandem and have long branched lobes, while in Opisthorchis the testes are semi-adjacent and are lobate. The life cycle of C. sinensis is typical of most trematodes apart from the schistosomes. Because of the multiplication of various larval stages in the snail, many thousands of cercariae emerge over the life of the snail for each miracidium which penetrated.

The infection is acquired through the consumption of raw, salted, pickled, smoked, marinated, dried, partially cooked, or poorly processed freshwater fish hosting metacercarial cysts in the subcutaneous connective tissues. Dogs are the most important reservoir hosts of *C. sinensis* and are usually responsible for perpetuating its transmission, even though human-snail-fish-human transmission can be preponderant in some areas; pigs and rats can also be naturally infected. O. viverrini is more zoophilic than C. sinensis and civet cats (family: Viverridae) are the natural reservoir hosts of the parasite (hence the name); infection is also common in domestic cats and dogs. Cats are important reservoir hosts of O. felineus, but infection is frequently found also in dogs, foxes, cats and pigs (Muller, 2002).

All the liver flukes have similar clinical manifestations, whose severity is proportionate to the number of worms infecting the host. The majority of infections are light and symptomless; in this case the presence of worms is only diagnosed at necropsy. Heavier infections (over 100 worms in humans) result in diarrhoea, fever, oedema, and swelling of the liver (hepatomegaly) and spleen (splenomegaly); there is also a high eosinophilia (up to 40%). There can also be recurrent gallbladder colic due to expulsion of worms or stones, associated with recurrent cholangitis and loss of weight (see Georgi and Georgi, 1992 for effects in dogs). Pathologically the adult flukes cause proliferation of the bile duct epithelium, followed by fibrosis of the ducts and destruction of the adjacent liver

Table 7.1. Trematodes reported from both humans and dogs. \* = rare. As far as possible the authorities quoted are recent, accessible publications which review the infection.

Parasite	Intermediate hosts	Final hosts	Distribution and location in host (reference)
Family Cathycotylidae			
Prohemistomum vivax	1. <i>Cleopatra</i> 2. Brackish water fishes	Kite, dog*, cat, man (once)*	Egypt Small intestine (Nasr, 1941)
Family Diplostomatidae			
Alaria alata	1. <i>Planorbis (?)</i> 2. Frogs	Dog, cat, fox, man (larvae)*	USA, Canada, Europe, Mid. East Small intestine (Dalimi and Mobedi, 1992)
A. americana	1. <i>Planorbis</i> 2. Frogs and snakes	Cat, dog, fox, man (larvae)*	SW USA, Canada <b>Small intestine</b> (Freeman <i>et al.</i> , 1976)
A. marcianae	1. <i>Planorbis</i> 2. Frogs and snakes	Cat, dog, coyote, fox, man (larvae)*	SW USA, Canada Small intestine (Shoop and Corkum, 1983a, b)
Family Echinostomatidae	Ū.		
Echinochamus fujianensis	1. Bellamya	Dog, cat, pig	China Small intestine (Yu and Mott, 1994)
E. japonicus	1. <i>Parafossarulus</i> 2. Fw fish and frogs	Heron, dog, cat, man	China, Japan, Taiwan Small intestine (Lin, 1985)
E. liliputanus	1. Snails 2. Fw fish or none	Dog, man	China <b>Small intestine</b> (Xiao <i>et al.</i> , 1994)
E. perfoliatus	1. <i>Lymnaea, Bithynia</i> 2. Fw fish	Dog, cat, fox, pig, man	Japan, Taiwan, Europe Small intestine (Lu, 1996)
Echinoparyphium recurvatum	1. <i>Lymnaea, Planorbis</i> 2. As above	Domestic birds, man (exper. dog, cat)	Taiwan Small intestine (Lu, 1982)
Echinostoma angustitestis	1. Snail 2. Fw fish	Dog (exper.), man*	China <b>Small intestine</b> (Chen <i>et al.</i> , 1992)
E. cinetorchus	1. Segmentina 2. Snails, frogs	Domestic birds, dog, cat, man	Japan, Korea, Taiwan <b>Small intestine</b> (Ryang <i>et al.</i> , 1986)
E. hortense	1. <i>Lymnaea</i> 2. Fw fish	Cat, rats, dog, man	China, Japan, Korea Small intestine (Tani, 1976)
E. ilocanum	1. <i>Hippeutis</i> 2. Snails	Dog, cat, man	Philippines, Malaysia China, Indonesia Small intestine (Geerts <i>et al.</i> , 1987)
E. malayanum	1. <i>Lymnaea</i> 2. Snails, fish	Pig, rat, man (exper. Dog)	China, India, Indonesia Small intestine (Lie-Kian and Virik, 1963)
E. revolutum	1. <i>Helisoma</i> 2. Snails	Domestic birds, man, muskrat, (exper. dog)	Indonesia, Taiwan <b>Small intestine</b> (Lu, 1982)

Episthmium caninum	1. Snails? 2. Fw fish	Dog, man*	Thailand Small intestine (Radomyos <i>et al.</i> , 1991)
Family Dicrocoeliidae			
Dicrocoelium dendriticum	1. <i>Helicella</i> 2. Ants	Most herbivores, dog*, man*	Europe, Asia, Africa, Americas <b>Bile ducts</b> (Petithory and Ardoin, 1990)
Family Fasciolidae			
Fasciolopsis buski	1. <i>Hippeutis</i> 2. On plants	Pig, man, dog	Bangladesh, India Cambodia, China, Vietnam, Laos, Malaysia, Taiwan, Thailand Small intestine (Kumar, 1987)
Family Heterophyidae			
Apophallus donicus	1. <i>Flumenicola</i> 2. Fw fish	Heron, fox, dog, cat, (exper. man)	East Europe, Canada Small intestine (Niemi and Macy, 1974)
Centrocestus armatus	1. Semisulcospira	Fish-eating birds, dog, cat (exper. man)	Japan
	2. Fw fish		Small intestine (Hubbert et al., 1975)
C. formosanus	1. Semisulcospira, Melania	Fish-eating birds, dog, cat, rat, man	China, Japan
	2. Fw fish, frogs		Small intestine (Cheng et al., 1991)
Cryptocotyle lingua	1. Tantoglabrus	Fish-eating birds and mammals, dog,	Greenland
	2. Marine fish	cat, man*	Small intestine (Rausch et al., 1967)
Haplorchis pumilio	1. Melania	Fish-eating birds, dog, cat, man	Philippines, Laos, Egypt
	2. Fish ( <i>Puntius</i> )		Small intestine (Giboda <i>et al.</i> , 1991)
H. tachui	1. Melania	Cattle, dog, cat, man	Philippines, Laos, Egypt
	2. Fish		Small intestine (Tadros and El-Mokkadem, 1983)
H. yokogawai	1. Stenomelania	Fish-eating birds, cattle, dog, cat, man	Philippines, Indonesia, Hawaii, Egypt
	2. Fish		Small intestine (Kwo En Hoa and Lie Kian Joe, 1953)
Heterophyes dispar	1. Pirenella	Fish-eating mammals, fox, dog, cat, man	Korea
	2. Marine fish	Fish astimum and for dealers at more	Small Intestine (Chal and Lee, 1990)
H. neteropnyes	1. Pirenella, Ceritnidea	Fish-eating mammals, fox, dog, cat, man	Egypt, Japan, Korea, France
l latavanhuanaia aantinus	2. Brackish w fish	Dec. and man	Small Intestine (Murrell, 1995)
Heterophyopsis continua	1. Certinidea?	Dog, cat, man	Japan, Korea
Mataganimus vakagawai		Fich acting birds dag	Small Intestine (Charland Lee, 1990)
Metagonimus yokogawai	2. Fw fish	cat, rat, man	(Murrell, 1995) Brazil
			Small intestine (Chieffi et al., 1992)
Phagicola longa	1. Snails?	Fish-eating birds, dog*, man*	Egypt
	2. Mullet		Small intestine (Shalaby and Trenti, 1994)
			Continued

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Table 7.1.	Continued.
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Parasite	Intermediate hosts	Final hosts	Distribution and location in host (reference)
P. ornamentata	1. Snails?	Man? (exper. dog)	Egypt
	2. Tilapia		Small intestine (Shalaby et al., 1994)
P. ornata	1. Snails?	Man? (exper. dog)	Egypt
	2. Tilapia		Small intestine (Shalaby et al., 1994)
Pharyngostomum flapi	1. Snails?	Man? (exper. dog)	Philippines, Egypt
	2. Tilapia		Small intestine (Shalaby and Trenti, 1994)
Procerovum calderoni	1. Melania, Thiara	Man (exper. dog, cat, chicken)	Japan
	2. Fw fish		Small intestine
P. varium	1. Snails?	Heron, man* (exper. dog)	Korea
	2. Fish		Small intestine (Chai and Lee, 1990)
Pygidopsis summa	1. Tympanotus	Fish-eating birds, dog, cat, man*	Hawaii, Philippines, Thailand, Korea, Japan
	2. Brackish w fish		Small intestine (Radomyos et al., 1994)
Stellantchasmus falcatus	1. Stenomelania	Fish-eating birds, dog, cat, rat, man	Korea, Thailand
	2. Brackish w fish		Small intestine (Chai et al., 1988)
Stictodora manilensis	1. Pirenella?	Dog, man (once)*	Egypt
	2. Mullet, goby		Small intestine (Shalaby and Trenti, 1994)
Family Lecithodendriidae			
Moedlingeria	1. Snails?	(Exper. dog) man?	Indonesia, Thailand
amphoraeformis	2. Tilapia		Small intestine (Bhaibulaya, 1982; Radomyos et al., 1994)
Phaneropsolus bonnei	1. Bithynia?	Man, dog	Thailand
	<ol><li>Insect larvae, fw fish</li></ol>		Small intestine (Hinz, 1996)
P. spinicirrus	1.?	Primates, man*, dog?	Thailand
	2. Insect larvae		Small intestine (Bhaibulaya, 1982; Hinz, 1996)
Prosthodendrium	1. Bithynia?	Rat, bat, dog*, cat, man*	Thailand, Indonesia
glandulosum	2. Insect larvae		Thailand <b>small intestine</b> (Bhaibulay, 1982; Radomyos et al., 1994)
P. molenkampi	1. Bithynia?	Primates, man, dog?	Thailand
	2. Insect larvae		Small intestine (Hinz, 1996)
P. obtusum	1. Bithynia	Rat, bat, dog*, cat, man*	Japan
	2. Insect larvae		Small intestine (Smales et al., 1990)
Family Microphallidae			
Microphallus minutus	1. Snails?	Dog, rat (exper. man*)	Brazil, Ecuador, Panama, USA
	2. Shrimp		Bile and pancreatic ducts (Dill, 1993)

# Family Opisthorchidae

Amphimerus pseudofelineus (= Opisthorchis guavaguiensis)	1. Snails? 2. Fw fish?	Coyote, dog, cat, man*	Alaska, Russia, France, Turkey Iran Bile ducts? (Dalimi and Mobedi, 1992)
Metorchis albidus	1. <i>Bithynia</i> 2. Fw fish	Fish-eating mammals, dog, cat, man	Canada, Greenland Bile ducts? (Maclean <i>et al.</i> , 1996)
M. conjunctus	1. <i>Amnicola</i> 2. Fish	Fish-eating mammals, dog, cat, man	Vietnam, Japan, Korea, China, Taiwan Bile and pancreatic ducts (Kumar, 1987)
Clonorchis (= Opisthorchis) sinensis	<ol> <li>Bulimus, Parafoss- Arulus</li> <li>Cyprinid fish</li> </ol>	Man, cat, dog, pig, fish-eating carnivores	Russia, Siberia, Central Europe <b>Bile ducts?</b> (Lebedev, 1990)
Opisthorchis felineus	1. <i>Bithynia</i> 2. Fw fish	Cat, dog, pig, fox, man	India Gall bladder (Leiper, 1913)
O. noverca	1.? 2.?	Pig, dog*, man*	Thailand, Laos <b>Bile ducts</b> (Hinz, 1996)
O. viverrini	1. <i>Bythnia</i> 2. Fw fish	Civet cat, dog, man	Italy, Russia, Portugal, Germany Bile ducts (Semenova and Ivanov, 1990)
Pseudamphistomum truncatum	1. Snails 2. Fw fish	Fish-eating mammals, dog, cat, man	Cameroon, Gabon, Nigeria, E. Guinea Lungs (Khalil, 1991)
Family Paragonimidae			
Paragonimus africanus	1. Snails? 2. Crabs	Civet cat, dog, man, mongoose	Thailand, China, Laos Lungs (Kino <i>et al.</i> , 1995; Hinz, 1996)
P. heterotremus	1. Tricula 2. Crabs	Cat, dog, rat, man	China Lungs (Chung <i>et al.</i> , 1977)
P. hueit'ungensis	1. <i>Tricula</i> 2. Crabs	Cat, dog, man*	Canada, USA Lungs (Dubey, 1979)
P. kellicotti	1. <i>Pomatiopsis</i> 2. Cravfish	Wild carnivores, cat, dog, pig, man*	Mexico, Peru, Central America, Ecuador Lungs (Argumedo, 1989)
P. mexicanus	1. <i>Araopyrgus</i> 2. Crabs	Wild carnivores, opossum, cat, dog, man	Japan Lungs (Sugano <i>et al.</i> , 1989; Nishida, 1989)
P. miyazakii	1. Bythinella 2. Crabs (Potamon)	Wild carnivores, cat, dog, man*	Philippines Lungs (Ito <i>et al.</i> , 1979) Taiwan, Korea, Japan lungs (Miyazaki, 1978)
P. philippinensis	1. <i>Antemelenia</i> 2. Crabs ( <i>Sesarma</i> )	Man (exper. dog, rat)	China Lungs (Wang <i>et al.</i> , 1985)
P. pulmonalis	1. <i>Semisulcospira</i> 2. Crabs etc.	Cat, dog, man*	Cameroon, Nigeria, Liberia Lungs (Sachs and Cumberlidge, 1990)

Continued

Table 7.1.	Continued.
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Parasite	Intermediate hosts	Final hosts	Distribution and location in host (reference)
P. skrjabini	1. <i>Tricula</i>		Asia, Russia
P utorobilatorolia	2. Clabs	Polm sivet est des mon*	Lungs (Tokogawa, 1965, 1969)
F. UlerOblialeralis	1. Allopollius?	Faim civel, cal, dog, man	Sapari, Chilla, Kolea, Nigeria
P westermani	1 Semisulcospira	Primates wild carnivores dog man	Janan China Korea Nigeria
1. Westerman	2 Crabs and cravitsh	T finales, wild carrivoles, dog, man	Small intectine (Acada at al. 1962)
Family Planiorchidae			
Plagiorchis muris	1 Lymnaea	Man dog cat pig wild carnivores	SWUSA
r lagioronio mano	2 Snails midge	Mari, dog, out, pig, wild ournivored	Mesenteric blood vessels (Lee 1962 Thrasher 1964)
Family Schistosomatidae	E. Challe, Mildgo		
Heterobilharzia americana	Lvmnaea	Rodents, birds, dog, sheep, man*	India. Thailand. Indonesia
	Snails, midge		Mesenteric blood vessel
	g-		(Agrawal and Shah, 1989)
Family Schistosomatidae			(
Heterobilharzia americana	1. Lymnaea, Pseudosucc-Nea	Rodents, birds, dog, sheep, man*	Indonesia, China, Philippines, Japan, Malaysia, Thailand
	2. None		Mesenteric blood vessel (Jordan et al., 1993)
Schistosoma incognitum	1. Radix	Dog, wild Carnivores, man (larvae)	Africa, Caribbean, S. America
Ũ	2. None		Mesenteric blood vessels (Jordan et al., 1993)
S. japonicum	1. Oncomelania	Pig, sheep, dog, man (once)*	Cambodia, Thailand, Laos
	2. None		Mesenteric blood vessels (Bruce and Sornmani, 1980)
S. mansoni	1. Biomphalaria	Man, cattle, buffalo, dog	Congo, Burundi, Uganda
	2. None	-	Mesenteric blood vessels (Rollinson and Simpson, 1987)
S. mekongi	1. Neotricula	Man, primates, rodents, dog	USA
	2. None		Small intestine (Milleman and Knapp, 1970)
S. rodhaini	1. Biomphalaria	Man, dog	Siberia
	2. None	Rodents, dog*, man (once)*	Small intestine (Milleman and Knapp, 1970)
Family Troglotrematidae			
Nanophyetus salmincola	1. Goniobasis/Oxytrema	Fish-eating mammals, fish-eating birds,	
	2. Salmon	dog, cat, man	
N. salmincola schikhobalowi	1 <i>Semisulcospira</i> 2. Fw fish	Badger, mink, fox, dog, cat, man	

parenchyma; chronic infections can be associated with jaundice, portal hypertension, and ascites (Muller, 2002; Crompton and Savioli, 2007). Cancer of the bile ducts (cholangiocarcinoma) is strongly associated with both C. sinensis and O. viverrini infections and both agents are classified as 'carcinogenic to humans' by the International Agency for Research on Cancer (IARC) (Bouvard et al., 2009). Cholangiocarcinoma is a major cause of death among humans in endemic areas, and very probably occurs with other species, such as dogs and cats. In Russia and East Europe O. felineus is a common parasite of cats, and to a lesser extent dogs, but human infection only occurs occasionally except for areas of Siberia, where salted or smoked fish is habitually eaten raw. Human infection with this species is often accompanied by acute symptoms of high fever and abdominal pain, but a less severe chronic phase (Muller, 2002). O. felineus is listed as 'not classifiable as to its carcinogenicity to humans' (IARC, 2010).

*Metorchisalbidus* and *M. conjunctus* are two flukes normally parasitic in North American fish-eating mammals including dogs, wolves, and foxes, in which they are responsible for cholangiohepatitis and periductular liver fibrosis (Wobeser *et al.*, 1983; Muller, 2002). They occasionally occur in humans who eat raw fish. The latter species was responsible for infection in 19 people in Canada who suffered from upper abdominal pain, low-grade fever, and a high eosinophilia, lasting up to 4 weeks, who had all eaten sashimi in a restaurant. Praziquantel was very effective in treatment (Maclean *et al.*, 1996).

Amphimerus pseudofelineus causes cholangitis, pancreatic neoplasms, and abdominal distension in cats, treatable with high doses of praziquantel, but there is little information on its effect in dogs or humans.

#### The Heterophids

#### Superfamily Opisthorchioidea: Family Heterophyidae

The heterophyids are a group of minute hermaphroditic flukes usually measuring less than 2.5mm in length, with a body covered in spines. The adults live among the crypts of the small intestine attached to the epithelial cells and can be easily missed at necropsy. They are all very similar morphologically and have almost indistinguishable, small (26  $\times$ 15 µm) operculate eggs, containing a miracidium when passed out in faeces. In freshwater the miracidia hatch, penetrate, and develop in appropriate species of snails where they multiply, and after a few weeks release cercariae. These encyst in several species of freshwater or brackish water fish (e.g. mullet, minnow, sweetfish) which, when eaten raw or undercooked, pass on the infection. Because the eggs are difficult or impossible to differentiate, reliable data on infection with the different species are lacking. Most species are parasites of fish-eating carnivores (e.g. dogs, foxes, wolves, jackals, cats) or birds (e.g. pelicans) and have almost identical life cycles. They are mainly prevalent in South-East Asia and the Mediterranean basin. Twenty infections have been reported from both humans and dogs (Table 7.1).

Heterophyes heterophyes and the very similar Metagonimus yokogawai are the most common species which infect humans and dogs. They both measure 1.0–1.7 mm in length and differ mainly in that the former species has an accessory genital sucker near the ventral sucker. The adults live in the mucosal crypts of the duodenum and jejunum, and produce superficial inflammation and necrosis with excessive secretion of mucus. In light infections they are usually asymptomatic, but in heavier infections the clinical picture may resemble that of amoebiasis, with diarrhoea, nausea, and intense griping pains. Occasionally worms penetrate very deeply into the crypts close to large lymphatics and blood vessels; in this case eggs may be carried and found in different tissues. Location in the CNS and heart valves can be severe and might be fatal, as in the case of humans dying of congestive heart failure. An adult Heterophyes has also been recovered from the heart (Collomb et al., 1960). Eggs of another species, Haplorchis pumilis, have been recovered from the spinal cord, producing transverse myelitis, with loss of motor and sensory function (see Guttierez, 1990). In the Nile

Delta region of Egypt, human infection with *Heterophyes* is associated with eating pickled mullet at the feast of *Sham-al-Nessim*, and there is a high infection rate in children and young adults.

Many other species of the family Heterophyidae are common in areas of South-East Asia, where expulsion of adult worms or detection of eggs from faecal examinations is commonly reported. They are frequently referred to by the generic term 'minute intestinal flukes' (Sripa *et al.*, 2010). Dogs, cats, and rats are the most frequent natural hosts; these infections are characterized by a varying degree of pathogenicity, from very mild to lethal (Chai *et al.*, 2009a).

#### **The Paragonimids**

## Superfamily Plagiorchioidea: Family Paragonimidae

The paragonimids are almost globular hermaphroditic trematodes, most measuring about 12mm in length and 6mm in width, with small suckers and symmetrical lobed testes in the posterior part of the body. They live in pairs in cysts in the lung, and crustaceans act as second intermediate hosts. Many species occur in carnivores (mainly felids, but also dogs, pigs, and monkeys) throughout the world but most of the estimated 22 million human infections are caused by *Paragonimus* westermani in South-East Asia (Toscano et al., 1995; Fürst, 2012), as this is the main part of the world where crustaceans are eaten uncooked. Many other species which can also infect humans (Table 7.1) can be distinguished by (often slight) morphological and life-cycle differences. The most common are P. heterotremus in South-East Asia, P. philippinensis in the Philippines; P. uterobilateralis and P. africanus in Africa: and *P. mexicanus* in Central and South America.

Eggs of paragonimids, measuring about  $100 \times 50 \,\mu$ m, are produced by the adult worms in the lungs and are conveyed up the trachea and passed out in the sputum or are swallowed and escape in the faeces. Once an egg reaches freshwater a miracidium

larvae develops inside it within a few weeks, emerges, and enters a suitable species of snail. After the usual multiplicative stages in the snail, the cercariae emerge and enter freshwater crabs or crayfish. When the infected crustacean is eaten raw, salted, pickled, smoked, marinated, dried, partially cooked, or poorly processed, the metacercarial larvae excyst and reach the lungs after penetrating through the intestinal wall, the diaphragm, and lung capsule. In China 'drunken crabs' are steeped in rice wine before eating, in the Philippines crab juice is a delicacy, while in Korea crayfish juice is used as a cure for measles in children.

The developing worm pairs in the lung provoke inflammatory and granulomatous reactions around them to form a cyst which can be in communication with a bronchiole. Fully formed cysts measure about 20mm in diameter. Eventually the contained worms die and the cysts become fibrotic and calcify. Even though early or light infections can be asymptomatic, paragonimiasis is typically associated with considerable morbidity: the most common presentation is that of a chronic pulmonary disease with fever, cough, dyspnoea, chest pain, and pneumothorax; rusty sputum is a classical finding. Such clinical picture is often mistaken for tuberculosis (Toscano et al., 1995), although the patient appears to be healthier than in the latter infection.

In general, human infection caused by the rarer, more clearly zoonotic species, tends to have worms occupying ectopic locations: *P. mexicanus*, a New World species (Table 7.1), is particularly likely to cause cerebral paragonimiasis, a condition more common in children, occurring when larvae migrate out of the lungs, along the soft tissues to the brain, and become foci for abscesses. Cerebral paragonimiasis gives rise to symptoms resembling epilepsy, a cerebral tumour, or a stroke, such as severe headache, seizures, sensory and motor impairment, and cognitive disorders. The organs or the wall of the abdominal cavity and the subcutaneous tissues represent other sites of ectopic paragonimiasis. Treatment is with praziquantel or triclabendazole, and diagnosis by finding the eggs in sputum or faeces; immunological tests have been experimentally developed but are not commercialized.

Susceptible species of crabs and crayfish live in fast-flowing mountain streams, and in most parts of the world these are not eaten raw. Consequently human infections in Africa and the Americas are rarer than in Asia, and occur predominantly in individuals from remote areas. *P. westermani* and *P. heterotremus* can also infect rodents and these can act as paratenic hosts for cats and dogs, since the worms do not usually develop fully in them.

P. kellicotti is the only species endemic to North America. It is a parasite of wild and domestic animals, including dogs and cats, but can also cause infection in humans (Procop, 2009); a thorough review of cases of paragonimiasis that occurred in the United States has been recently conducted by Fried and Abruzzi (2010). In dogs, X-rays showed saccular bronchial dilatations after 2–3 weeks. often with pneumothorax and distinct airfilled cavities measuring 20-30mm after 4 weeks. These conditions sometimes resolved, but treatment with fenbendazole, albendazole, or praziquantel were all effective (Dubey, 1979). More recently, triclabendazole has also shown to be effective. A cough is typical of infections with paragonimids in dogs.

# The Troglotrematids

#### Superfamily Plagiorchioidea: Family Troglotrematidae

This group is related to the paragonimids and most species do not inhabit the alimentary tract (occupying body sinuses, kidney, and liver), although the one species occasionally found in man is intestinal. They differ from the paragonimids in that the genital pore is posterior to the ventral sucker and there is a cirrus sac.

*Nanophyetus salmincola* is an intestinal parasite of fish-eating wild carnivores (e.g. wild bears and raccoons), birds and canids (including red foxes and domestic dogs) in Siberia and the Pacific north-west of the United States (Table 7.1). Eggs are passed out in the faeces and the miracidia which develop inside the egg then hatch in freshwater and penetrate suitable species of snails. Asexual

multiplication occurs in the snail, and the cercariae which emerge form cysts in various tissues, particularly the kidney, of salmonid fishes. Infection follows ingestion of parasiteinfected fish, and is usually non-pathogenic. However, in dogs in the United States, the parasite is known for its association with 'salmon poisoning' of dogs and other canids, which is caused by a rickettsial organism, Neorickettsia helminthoeca, for which the trematode acts as a vector (Milleman and Knapp, 1970). 'Salmon poisoning' results in a haemorrhagic enteritis with high fever, anorexia, vomiting, and lymphadenopathy; there is a high mortality occurring 10-14 days after infection. The rickettsia has not been reported from humans but it is possible they may be susceptible. Following ingestion of raw or insufficiently cooked salmon, some patients in Russia and the United States suffered from diarrhoea with weight loss, nausea, vomiting, fatigue, anorexia, and a high eosinophilia (43%). Symptoms usually resolved after a few months. One case also had a high fever but the possible role of a rickettsia was not investigated (Eastburn et al., 1987). Diagnosis in both hosts is by finding the characteristic unembryonated eggs, measuring about  $80 \times 45 \,\mu\text{m}$ , in the faeces.

Prevention is by not eating raw or smoked salmon and not feeding it to dogs. There has also been one case of infection through handling fish (Harrell and Deardorff, 1990). A 4.2% human infection rate has been reported from a focus on the lower Amur River in Siberia (Bernshtein *et al.*, 1992). Treatment with praziquantel is effective (Fritsche *et al.*, 1989). Wild carnivores act as reservoir host for both humans and dogs.

Lecithodendriids (Superfamily Plagiorchioidea: Family Lecithodendriidae) are usually intestinal parasites of insect-eating mammals, particularly bats. They are minute flukes recognizable by the fact that the gonads and vitelline body are in the forebody region. *Phaneropsolus* is the only genus regularly found in man and dogs, although there are other occasional parasites (Table 7.1). In a region of Thailand, adults of *P. bonnei* were recovered from 15% of inhabitants, and adults of *Prosthodendrium molenkampi* from 19% (Radomyas *et al.*, 1994). *P. molenkampi* has also been reported from Laos (Chai *et al.*, 2009b). Larvae, particularly those of dragonflies, act as second intermediate hosts. Pathogenicity is unknown, nor is it known how the final hosts are infected; presumably the parasites infect humans in areas where insects are eaten as delicacies or by accidentally ingesting insect larvae in water or on edible vegetation. It appears unlikely that dogs are the normal definitive hosts for *P. bonnei*.

A number of plagiorchids (Superfamily Plagiorchioidea: Family Plagiorchidae): Plagiorchis harinasutai, P. javensis, P. muris, P. philippinensis, and P. vespertilionis have been reported from the intestine of man in Indonesia, Korea, Japan, Thailand, and the Philippines. They are about 3.0mm in length and are natural parasites of mammals feeding on aquatic insects (e.g. wild mice and cats, bats); they have also occasionally been recovered from dogs (Dalimi and Mobedi, 1992). The second intermediate hosts for humans and dogs are probably freshwater fish, although a number of species have been shown to be variously involved in the parasite's life cycle, including snails, dragonflies, mosquitoes, and midges (Coombs and Crompton, 1991; Chai et al., 2007).

#### **The Fasciolids**

#### Superfamily Echinostomatoidea: Family Fasciolidae

These are large spiny trematodes with a flattened body and deeply lobed testes. The best known members of this family, the cattle and sheep liver flukes, Fasciola hepatica and *F. gigantica*, can be important human parasites in some parts of the world. The only member found in both humans and dogs is the giant intestinal worm, Fasciolopsis buski. The most important reservoir host for this trematode is the pig, followed by the buffalo, dogs only rarely becoming infected. This is primarily because there is no second animal intermediate host, the cercariae forming metacercarial cysts on water plants. Some of these, including the water bamboo, water caltrop, water chestnut, water hyacinth, and watercress

are eaten by people in many parts of Asia (Chai et al., 2009a): others are fed to pigs. Transmission is particularly intense in areas where water plants are cultivated in ponds that are fertilized by untreated pig or human faeces. The large adult worms, measuring up to 70mm, attach by their suckers to the wall of the small intestine. The eggs, measuring  $130 \times 80 \,\mu\text{m}$ , pass out in the faeces and on reaching freshwater a miracidium develops inside within about 1 month. Light infections are often asymptomatic, but large numbers of worms, which can be many hundreds, cause inflammation and ulceration of the intestinal mucosa with excessive production of mucus. Clinically, there is anorexia, nausea, acute abdominal pain, and possible facial oedema due to toxins produced by the parasite. Children in particular get infected by removing the outer covering of fruits or nuts with their teeth. Treatment is by praziquantel or albendazole.

# The Echinostomatoidea

## Superfamily Echinostomatoidea: Family Echinostomatidae

Echinostomes are all parasites of the small intestine, and measure a few millimetres in length. They have an oval or elongate body and the tegument is covered with spines. The most characteristic feature is the presence of a collar behind the oral sucker with a single or double crown of longer spines. Both suckers are well developed. Most species are parasites of birds but some are natural parasites of mammals and most also have a wide host range.

The characteristic eggs of echinostomes are relatively large, measuring about 100 × 65  $\mu$ m, although it is difficult to tell them apart. The second intermediate hosts (in addition to the snail first intermediate host) are large edible types of snail, amphibians, or fish (Table 7.1). In the definitive host, heavy infections with mature worms produce an inflammatory reaction of the mucosa and ulceration at the site of attachment, and there may be diarrhoea, nausea, and intestinal colic in the morning, relieved by food. Treatment is with praziquantel.

*Echinostoma ilocanum* is a common parasite of dogs in Canton and was first reported from prisoners in jail in Manila in 1907. Occasional human cases have been reported since from the Philippines, China, Malaysia, Indonesia, Thailand, and India. Infection is contracted from eating uncooked large edible snails (e.g. *Pila* or *Vivipara*) containing metacercariae. Among the other echinostomes whose natural definitive hosts are dogs, it is worth remembering here *Echinostoma hortense* and *E. malayanum*, both of which are common in east and South-East Asia.

#### The Diplostomes

#### Superfamily Diplostomoidea: Family Diplostomatidae

In this group the body is divided into two regions, with a wide flattened, concave, anterior portion and a cylindrical posterior portion. Most are parasites of birds, but members of the genus *Alaria* parasitize mammals. The cercariae form metacercarial cysts in fish or amphibians.

Alaria americana and A. marcianae are two very similar species which are intestinal parasites of carnivores in North America, where they are found in raccoons, weasels, red foxes, badgers, cats, and occasionally dogs. They both have very similar, unusual, life cycles and are often considered as the same species, but Pearson and Johnson (1988) regarded them as distinct. Thus in the older literature it is not always clear which species is being referred to.

The life cycle of (presumably) *A. marcianae* has been elucidated from experimental infections in carnivores and rodents (Shoop and Corkum, 1983a, b; Smyth, 1995). If eggs from faeces reach water, the miracidia hatch out, and penetrate and multiply in suitable species of snails (probably including *Heliosoma* spp.). Cercariae which emerge develop in amphibian tadpoles where they develop into an unusual larval stage known as a mesocercaria. Basically, this is an enlarged cercaria with the penetration glands, but a more complex excretory system. Adult frogs and snakes act as carrier or paratenic hosts by ingesting tadpoles. When these are ingested by young carnivores, mesocercariae penetrate through the intestinal wall and diaphragm to reach the lungs. After developing into metacercariae in the lungs they are coughed up and become adults in the small intestine, producing eggs in about 20 days. The adults attach to the villi in the small intestine but cause little damage. However, in pregnant cats and dogs, the mesocercariae migrate to the mammary glands and infect suckling kittens or puppies. They can continue to infect subsequent litters until the larvae are all depleted. In the neonates the parasites develop into adults. The process was termed 'amphiparatenesis' by Shoop (1994). A pregnant callitrichid monkey has been infected experimentally and a similar situation ensued. This has serious implications for zoonotic human infections (Shoop, 1990).

While A. americana and A. marcianae are rare parasites in both dogs and humans, they are potentially very dangerous ones. A fatal case in Canada occurred in a man who ingested frogs' legs while hiking (Freeman et al., 1976). He was thought to be suffering from gastric flu but died 9 days later from extensive pulmonary haemorrhage, and at autopsy was found to have mesocercariae in many tissues. They probably penetrated the stomach wall and migrated to the lungs and other tissues both directly and by the circulatory system. Mesocercariae have also lodged in the eyes of both humans and dogs, causing neuroretinitis (at least in the former). An extensive review of human cases of infection with Alaria spp. occurring in the United States has been carried out by Fried and Abruzzi (2010).

*A. alata* is a European species frequently found in the small intestine of wild and domestic canids feeding on frogs. Its life cycle is similar to that of other *Alaria* spp., and larvae have been found in humans. Human infection is mainly related to the consumption of undercooked wild boar meat that contains the parasite's metacercariae in muscle or fat tissues (these are also known as Duncker's muscle flukes). Symptoms are usually mild (Shoop, 1994). *A. nasuae* has been identified in wild carnivores and in domestic dogs in Mexico although, so far, not in humans (Shoop, 1989; Shoop *et al.*, 1989).

# The Dicrocoelioidea

# Superfamily Dicrocoelioidea: Family Dicrocoeliidae

Dicrocoelium dendriticum is a cosmopolitan parasite of the biliary ducts of sheep and cattle, which utilizes terrestrial snails as intermediate hosts. Snails ingest the parasite eggs containing miracidia and release cercariae which are then ingested by ants. Herbivores become infected by ingesting ants containing metacercariae which alter the ants' behaviour so that they attach to grass leaves and increase the chances of ingestion. It is probable that most reported cases in humans and particularly in dogs are spurious, the eggs having been found in the faeces following ingestion of infected liver. Genuine human infection, also called lancet fluke infection, follows ingestion of infected ants and results in disturbed liver function, biliary tree disease, and a high eosinophilia (Mohamed and Mummery, 1990).

A historical review on information available on *Dicrocoelium* spp. has been carried out by Le Bailly and Bouchet (2010).

*Prohemistomum vivax* (Superfamily Strigeoidea: Family Cathycotylidae) is a parasite of fish-eating birds reported from Egypt and Japan. There has been one reported human case, when 2000 adult worms were recovered from the small intestine, and it has been found a few times in dogs.

### Conclusions

It is clear that infection with all trematodes apart from the schistosomes is based on dietary habits, and human prevention is by thorough cooking of fish, crustaceans, snails, amphibians, or snakes, and possibly by avoidance of eating insects. Dogs are not nearly as important as reservoir hosts for most of these parasites, as are cats, because they are not as likely to eat these intermediate hosts. Avoidance of schistosome infections is by not entering ponds, canals, or streams containing cercariae released from snails: not an easy task for humans living in endemic regions, particularly for children, fishermen, and farmers, or for dogs.

#### Note

<sup>1</sup> Adapted from the first edition, written by Ralph Muller. This chapter has been submitted in his memory.

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# **8** Dogs and Cestode Zoonoses

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The domestication of the dog some 12,000-14,000 years ago has undoubtedly been of great benefit to humans. From a Darwinian perspective, wolves that started to cohabit with humans made a smart choice, given the nearly ubiquitous distribution of dogs around the world today compared to the patchy distribution and small population of wolves. The human:dog relationship may be as close as pampered and cosseted lap dogs, to strays and feral dogs which live a precarious existence on the fringes of human society. The diversity of breeds of dogs and uses to which we put them may lead to their exposure to infectious organisms and their unwitting participation in the transmission of over 60 zoonotic infections (Baxter and Leck, 1984; Hubbert et al., 1975). Human behaviour plays a pivotal role in the perpetuation of tapeworm or cestode infections in dogs and their zoonotic importance in humans, being transmitted through the inadvertent ingestion of eggs (Macpherson et al., 2000; Macpherson, 2005).

This chapter reviews the complex role dogs play in the cestode zoonoses, with a focus on the most important from a public health point of view, including *Echinococcus* granulosus and *E. multilocularis*, to less common *Echinococcus* spp., *Diphyllobothrium* spp., *Dipylidium* sp., *Taenia* spp., *Spirometra* spp. and *Mesocestoides* spp.

# Echinococcus spp.

The genus Echinococcus comprises a complex of species and sub-species which is undergoing taxonomic revision (Thompson, 2008). Possibly four species, (until recently all considered to be E. granulosus): E. granulosus sensu stricto, E. ortleppi, E. intermedius, and E. canadensis may cause cystic echinococcosis (CE) in humans, livestock, and some wild animal species. E. equinus (previously E. granulosus horse strain) appears to transmit between equids and dogs and is not zoonotic. E. multilocularis causes human alveolar echinococcosis (AE). Both CE and AE are of major public health importance. The dog is the main definitive host of *E. granulosus, E. ortleppi, E. intermedius,* and E. canadensis, and dogs are becoming increasingly recognized as a source of human infection with E. multilocularis. Two other species of Echinococcus, E. vogeli and E. oligarthrus, are geographically limited to Mesoamerica and South America and rarely cause disease in humans. Dogs play a role in the transmission of *E. vogeli* to humans. Felids are the main definitive hosts of *E. oligarthrus*, and dogs play no part in the transmission of this species, which will not be considered further.

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# *Echinococcus granulosus* (Batsch 1786) and Other Related Species

The taxonomy of *E. granulosus* is presently undergoing revision and a number of genotypes, previously recognized as strains of *E. granulosus*, are likely to be separate species based on molecular evidence (see Table 8.1).

# Dogs as definitive hosts of *Echinococcus granulosus*

Although susceptibility between – and even within – different breeds occurs, globally dogs are definitive hosts *par excellence* for *E. granulosus*. Dogs and other suitable carnivores become infected when they ingest protoscoleces found in hydatid cysts. These are most commonly found in the liver or lungs, and to a lesser extent in any other internal organ, of an enormous range of domestic and wild mammalian intermediate host species. The protoscoleces evaginate in the small intestine, and the rostellum of the scolex attaches to the base of the crypt of Lieberkühn, and the suckers attach to the base of the intestinal villi. The adults grow to a length of between 2 and 11 mm, and are hermaphrodites. The prepatent period varies between 34 and 58 days (Thompson, 1995).

#### Worm burden

The mean worm burden in dogs varies considerably between endemic localities, but in most endemic regions in developed countries (Europe, New Zealand, North America) worm burdens of around 200 are usually found (Gemmell *et al.*, 1987). Much heavier worm burdens have been reported in dogs living in many of the less developed regions of the world, which must increase the biotic potential of the parasite. This would be useful for the survival of the parasite in areas where the climatic conditions are inimical to the survival of the eggs (Wachira *et al.*, 1991). Heavy worm

Table 8.1. Latest proposal for the taxonomic revision of *E. granulosus*.

Proposed <i>Echinococcus</i> species	Previously recognized <i>E. granulosus</i> strains (genotypes)	Definitive hosts	Intermediate hosts	Infective to man	Geographic distribution
<i>E. granulosus</i> sensu stricto	Sheep strain (G1, G2, G3)	Dog, fox, dingo, jackal, hyena, Wolf	Sheep, cattle buffalo, pigs, camel, goats, macropods	Yes	Cosmopolitan: Eurasia, Africa, North and South America, Australia
E. equinus	Horse strain (G4)	Dog	Equines	No evidence	Europe, Middle East, South Africa,
E. ortleppi	Cattle strain (G5)	Dog	Cattle, buffalo, sheep, goats	Yes	Europe, South Africa, India, Nepal, Sri Lanka, Russia, South America?
E. intermedius	Camel strain (G6), Pig strain (G7), (G9)	Dog	Pigs, goat, camel, cattle	Yes	Middle East, Iran, Africa, China, Nepal Central Asia, Eastern Europe, Argentina
E. canadensis	Cervid strain (G8, G10)	Wolf, dog	Cervids	Yes, but relatively benign	Northern Eurasia, North America
E. felidis	Lion strain	Lion	Warthogs, zebra, cape buffalo, wildebeest	Unknown	East and southern Africa

burdens may exist due to a range of host factors including their heterogeneity, to susceptibility to infection due to immunological, genetic, nutritional, and other host factors. The lack of dog control measures where dogs breed frequently and have short life spans (Matter and Daniels, 2000) and would result in a largely immunologically naive population.

In Australia an infected wild dog (domestic dog and dingo hybrid) was found to harbour over 300,000 worms (Jenkins and Morris, 1991), and wild dogs in general tend to have heavy worm burdens (Jenkins et al., 2000). Heavy infections have also been reported in Kenya, where of 274 infected dogs examined in the Turkana District, 122 (44.5%), 54 (19.7%), and 98 (35.8%) had light (1-200); medium (201-1000); and heavy (>1000) worm burdens, respectively. Many of the heavily infected dogs had over 50,000 adults which completely carpeted the entire length of the small intestine (Macpherson et al., 1985). Fertility of hydatid cysts in Turkana is high both in humans (Macpherson, 1983) and livestock (Macpherson, 1981) which would facilitate heavy worm burdens in dogs. Heavy worm burdens have also been reported in the Levant country of Jordan where the heaviest worm load was 16,467 in a dog fed offal by a slaughterhouse worker (Kamhawi and Abdel-Hafez, 1995). In Iraq, the mean worm burden in 57 infected dogs was 1844, with 61.4% of the dogs having burdens of >1000 worms (Molan and Baban, 1992). The heaviest infected dog in this study harboured 15,182 worms. In Tunisia the mean worm burden of infected dogs has been recorded at over 2000 worms (Lahmar et al., 2001). Heavy worm burdens have not been reported from all dry endemic regions and have not been reported in most north African countries or the Middle East (Eslami and Hosseini, 1998; Ibrahem and Gusbi, 1997; Ouhelli et al., 1997). In Morocco the average number of worms in 34 infected dogs was 219 (Ouhelli et al., 1997).

#### Egg production, dispersal, and survival

Egg production may be synchronous or asynchronous, with proglottids being produced roughly every 2 weeks. Egg production may reach over a million a day. Expulsion of eggs has been shown to be continuous (Lahmar *et al.*, 2001) and last for at least 80 days (Heath and Lawrence, 1991).

The mechanisms for the dispersal of eggs are unclear but are likely to be a combination of a number of factors. These range from the movements of the proglottids away from the faecal mass to dispersal by water, wind, flies (especially blowflies), and other insects and birds. Most eggs remain within 180 m of their deposition but under certain circumstances eggs appear to be able to disperse over considerable distances. For example, eggs of *Taenia hydatigena* have been shown to move over 60 km upwind by the activities of birds and insects (Torgerson *et al.*, 1992, 1995).

Egg survival is dependent on temperature and relative humidity. At 7 °C and 21 °C eggs survive for over 200 and 50 days, respectively (Gemmell, 1977). At temperatures of over 40 °C survival is only a few hours, but is prolonged if the eggs are in water (Wachira *et al.*, 1991). In the hot, arid regions of the world transfer of eggs from dogs to intermediate hosts must be rapid to be successful. Infected dogs have been shown to produce 8470 eggs a day and 0.0033 of these eggs develop into viable cysts (Gemmell *et al.*, 1987). The longevity of the adult worm in dogs is unknown but is possibly 1–2 years.

# Diagnosis of Echinococcus granulosus in dogs

Identification of infected dogs may be important for diagnostic, epidemiologic, or control/ surveillance reasons. Almost all hydatid control programmes necessitate consideration of quantification of canine echinococcosis (Gemmell, 1990). Diagnosis is most effective by autopsy and examination of the small intestine, which is also the only accurate method of recording worm burdens. Ante-mortem diagnosis has been carried out for many years using arecoline purgation. Although this method is highly specific, it has many drawbacks including poor sensitivity, and it is biohazardous and logistically problematic with up to 20% of dogs failing to purge (Craig, 1997; Craig et al., 1995; Wachira et al., 1990). The sensitivity of arecoline purgation has been reported to be as low as 37% (Ziadinov et al., 2008). The development of Echinococcus spp. coproantigen ELISA tests has dramatically improved the capability of sensitive and highly specific ante-mortem diagnosis of *E. granulosus* in dogs (Allan et al., 1992; Deplazes et al., 1992; Torgerson and Deplazes, 2009). Specificity is around 96% and sensitivity >80% when worm burdens are greater than 50. Pre-patent infections are detectable by coproantigen ELISA, and antigen levels return to normal within 5 days post-treatment. Coproantigens remain stable in formol saline preserved samples and also in faecal samples left in the 'open' for up to 6 days (Jenkins et al., 2000). To date, coproantigen ELISA for E. granulosus has been used to screen sheep farm dogs in Wales, Uruguay, Australia, and Peru (Cohen et al., 1998; Jenkins et al., 2000; Moro et al., 1997, 1999; Palmer et al., 1996); nomadic community dogs in northwest China (Wang et al., 2001); stray dogs in Spain, Jordan, and Nepal (Baronet et al., 1994; Deplazes et al., 1992; El-Shehabi et al., 2000); and feral dogs and dingoes in Australia (Jenkins *et al.*, 2000). Coproantigen positive rates ranged from <5.0% to 46%. Differentiation between E. granulosus and E. multilocularis by coporantigen detection is presently not possible routinely, as most assays appear to be genus rather than species specific. A PCR-based DNA detection assay has been developed for *E. granulosus* (Stefanic et al., 2004) and a real-time multiplexnested PCR system has been developed for the simultaneous detection of E. multilocularis and host species directly from faecal samples (Dinkel et al., 2011).

# Treatment of *Echinococcus* granulosus in dogs

Since the 1970s the treatment of choice has been praziquantel, given in a single oral dose of around 5 mg/kg body weight. The drug is well tolerated by dogs and to date no drug resistance has been reported. Praziquantel is metabolized within 1 h and consequently reinfection may occur not long after treatment.

# Epidemiology and public health importance

Infections with E. granulosus occur worldwide. A so-called European form, primarily involving synanthropic hosts in its cycle, has a nearly cosmopolitan distribution (Rausch, 1993). This form is a major public health and economic problem in northern parts of the North American continent and Eurasia, and is probably the archetypal form (Rausch, 1993; Thompson, 2008; Thompson et al., 2006). The global burden of CE is substantial, with as much as \$2 billion lost annually, and an excess of 1 million disability-adjusted life years (DALYs) (Budke et al., 2006). Regions with good documentation, where a relatively high prevalence in defined geographical areas has been reported, include the whole Mediterranean area including Southern Europe, Egypt, Libya, Tunisia, and Morocco (Dakkak, 2010; Rausch, 1993; Schantz et al., 1995; Sadjjadi, 2006). Another focus occurs in Africa south of the Sahara in the semi-arid areas of East Africa, including Kenya, Uganda, Sudan, Ethiopia, and Tanzania and in the rural areas of Nigeria and South Africa (Macpherson and Wachira, 1997; Magambo et al., 2006). Large foci are also known to occur in the sheeprearing countries of South America (Moro and Schantz, 2006), including Uruguay (Carmona et al., 1998), Argentina (in the Patagonian Provinces of Rio Negro, Chubut, Santa Cruz, and Tierra del Fuego) (Frider et al., 1988, 1999; Perdomo et al., 1997); Brazil (Rio Grande do Sol); and the high sierra areas of Chile, Peru, and Bolivia (Ramirez, 1979; Schantz et al., 1995; Williams et al., 1971). They also occur in Eastern Europe (Bulgaria, Romania, Poland), Russia, Central Asian Republics (Kazakhstan, Uzbekistan, Kyrgyzstan, Mongolia, Tajikistan and Turkmenistan) (Torgerson et al., 2006), and parts of China (Craig et al., 1991, 1992; Wen and Yang, 1997; Wang et al., 2008).

#### Africa and the Middle East

There are three broad categories of dogs in this region of the world: feral or stray dogs, which usually comprise the largest population; working sheepdogs, used particularly in north Africa and in the Middle East to herd sheep; and pet dogs which are kept mostly for guarding property and in rural areas to protect against wild animals (see Chapter 1). Very few dogs are considered as household pets with no other function. Stray dogs usually are not very visible during the day, but emerge at night to scavenge from rubbish dumps and around human settlements. In many north African, Levant, and Middle Eastern countries, owned pet dogs are not restricted to the home area and are allowed to roam freely with stray dogs. Many authorities consider these dogs, together with strays, as the main sources of infection for livestock and humans (Kamhawi and Abdel-Hafez, 1995; Macpherson et al., 2003; Ouhelli et al., 1997). The generally high prevalence of E. granulosus in dogs in North Africa and the Middle East is thought to be also due to a lack of appreciation of the life cycle of the parasite by abattoir workers, butchers, meat inspectors, and dog owners, and the lack of infrastructure and the enforcement of regulations governing disposal of infected offal. Home slaughter, particularly for religious and special ceremonial events, occurs throughout the region and at such times meat inspection is not enforced. In Morocco, feeding of infected offal to dogs was found to occur in all areas and since between 70% and 90% of owned dogs are allowed to roam free, there exists ample opportunities for exposure to infection (Ouhelli et al., 1997). The religious teachings of Muslims advise that dogs are impure. 'If a dog licks from the utensils of anyone of you it is essential to wash it seven times'...'Angels do not enter a house where there is a dog'... 'The Prophet has ordered the killing of dogs, except for a hunting dog, or a sheep or cattle dog' – sayings of the Prophet Muhammad, related by Muslim, Ahmed, Abu Dawood, Al-Bukhari, and Al-Behaqi. Nevertheless Muslims still find that dogs are useful or even essential to guard the home or livestock, and so are kept in large numbers: there are thought to be over 3 million dogs in Morocco (National Laboratory for Epidemiology and Zoonoses, 1993) which has a human population of just over 26 million. Children throughout the Middle East and in North Africa regularly have contact with dogs, and in this region CE has a relatively high prevalence in

children below 15 years of age. Responsibility for feeding and looking after dogs in Morocco and in the region in general is usually left to women, and this increased contact may be partly responsible for the higher incidence of CE among women compared to men (Kachani *et al.*, 2003; Macpherson *et al.*, 2004; Ouhelli *et al.*, 1997; Shambesh *et al.*, 1992, 1999).

A history of dog ownership has been shown to be important in some areas. For example, CE patients in Beirut were 21 times more likely to have had a history of dog ownership than other Beirutis (Abou-Daoud and Schwabe, 1964). The use of dogs for hunting wild pigs by Christians and Druze people, and feeding the offal to the dogs, is thought to be a risk factor increasing the incidence of CE amongst these groups compared to Arabs in Israel (Yarrow *et al.*, 1991). One study in Jordan demonstrated an association between contaminated water supplies and human CE (Dowling *et al.*, 2000).

In sub-Saharan Africa, there are a number of wild carnivores which serve as definitive hosts in addition to domestic dogs, but it is unlikely that any of these wild species play an important role in human infection (Macpherson and Wachira, 1997). A number of prevalence studies have been conducted in different countries and these are presented in Table 8.2. As in North Africa and the Middle East, there are large numbers of stray dogs, and most owned dogs are free to roam and scavenge. Dogs are maintained for guarding from intruders and wild animals but are not generally used for herding. Dogs spend most of their day in their home area but are rarely trained or shown affection. There have been few attempts to control their numbers in any of the sub-Saharan countries, and dog populations are therefore restricted by food, water, and shelter availability (see Chapter 2). In urban areas dogs living close to abattoirs are often infected with E. granulosus (Wachira et al., 1993). In the hyperendemic focus among the nomadic pastoralists of East Africa, there are usually no veterinary and scarce medical and educational facilities, no abattoirs, little knowledge about the parasite, and food for dogs is scarce, so infected offal is invariably fed to dogs. In such areas droughts are common, and it is thought that animals that die in huge numbers during drought years are very

Country – location	Dogs examined	Percentage dogs infected	References
North Africa			
Algeria	172	9.9	Senevet, 1951
Egypt	570	3.9	Moch <i>et al</i> ., 1974
	510	1.6	Hegazi <i>et al</i> ., 1986
Libya	243	29.6	<sup>a</sup> lbrahem and Gusbi, 1997
Morocco (1920–1949)	331	1–70	<sup>a</sup> Ouhelli <i>et al</i> ., 1997
(1979–1985)	103	48.3	ªOuhelli <i>et al</i> ., 1997
1995	282	33.3	ªOuhelli <i>et al</i> ., 1997
Tunisia	348	22.7	Kilani <i>et al</i> ., 1986
		21	Lahmar <i>et al</i> ., 2001
			No reference available
			No reference available
Sub-Saharan Africa			
Chad – Central	117	3.4	Troncy and Graber, 1969
Kenya – Turkana	695	13–63.5	Macpherson et al., 1985
<ul> <li>Maasailand</li> </ul>	92	37	Ngunzi, 1986
– Nairobi	156	10	Wachira <i>et al.</i> , 1993
Mozambique – Maputo	643	0.5	Ferreira, 1980
Nigeria (in general)	549	1.2–6.5	Dada, 1979; Dada et al., 1979
			Dada, 1980
Somalia	-	23	Macchioni et al., 1985
South Africa – Pretoria	1063	0.9	Verster, 1979
Sudan – Khartoum	33	3	El-Badawi <i>et al</i> ., 1979
<ul> <li>Central</li> </ul>	25	51	Saad and Magzoub, 1986
– South	76	52.6	Eisa <i>et al</i> ., 1962
Tanzania – Maasailand	10	60	Macpherson <i>et al</i> ., 1989a

Table 8.2. Reported prevalence of Echinococcus granulosus in dogs in Africa.

<sup>a</sup> Review, summarizing data from numerous sources

important for creating ideal conditions for the rapid expansion of the infected dog population (Macpherson, 1994; Wachira *et al.*, 1990).

A lack of hygiene, the use of water holes for drinking water to which dogs have access, and where *E. granulosus* eggs survive longer (Wachira *et al.*, 1991) may be important sources of human infection. Additionally, the preparation of food where dogs lick up the remnants, and a close association of dogs with women in particular (Watson-Jones and Macpherson, 1988) allows almost ideal conditions for the continuous transmission of the parasite in this region. It is not surprising that there is a continuous exposure to infection, and the prevalence of CE increases with age (Macpherson *et al.*, 1987, 1989b).

#### Asia

From China (including Tibet), through Mongolia, Siberia, Kazakhstan, the central Asian Republics, Nepal, Bhutan, Pakistan, India to Iran, the dog is the principal definitive host of *E. granulosus* (Budke *et al.*, 2005; Schantz *et al.*, 1995; Shaikenov *et al.*, 1999; Torgerson *et al.*, 2003b; Ziadinov *et al.*, 2008). Over this huge area of grazing steppe and montane pastures dogs have traditionally been and continue to be associated with nomadic, seminomadic, and settled pastoral communities.

In China, six provinces or autonomous regions, including Xinjiang, Gansu, Ningxia, Inner Mongolia, Qinghai, and Tibet have the highest reported prevalences of CE (Craig *et al.*, 1991). Dogs are used as guards, particularly in the towns and cities, and as shepherd dogs in the vast sheep-rearing areas (Liu, 1993). Autopsy surveys of dogs revealed high rates of infection in Xinjiang (7–71%); Gansu (27%); Ningxia, (56%); and Quinghai (11–47%) (Yan, 1983; Yang, 1992; Zhang, 1983). Arecoline puragation has revealed prevalences of between 8% and 19% in western

Sichuan (Budke *et al.*, 2005). In the Xinjiang Uygur Autonomous Region between 1957 and 1991, 8.1% of 27,186 dogs were found to harbour *E. granulosus* infections, as determined by either autopsy or arecoline purgation (Liu, 1993). In this region home slaughter was an important risk factor, and infection rates in dogs were higher in pastoral than in agricultural areas. Kazakh, Mongolian, and Kyrgiz peoples, who are mostly pastoralists, have correspondingly higher infections in their dogs compared to Han, Hui, or Uygur ethnic groups. In western Sichuan male dogs, and dogs that were allowed to roam, had higher infection rates (Budke *et al.*, 2005).

In Kathmandu, Nepal, a coproantigen study revealed a prevalence of 5.7% (5/88) in domestic dogs living near the area of the city where livestock was slaughtered, and 1.8% (3/171) domestic dogs from all areas of the city (Baronet *et al.*, 1994). As is the case elsewhere in Asia there were a large number of street dogs, some of which were 'owned' by the community, each apparently with its own 'territory', and domestic and street dogs were allowed to roam freely and had access to livestock viscera.

In rural dog populations in Central Asian republics, prevalences can reach 20% or more (Torgerson *et al.*, 2003a; Ziadinov *et al.*, 2008) with working shepherd dogs having a greater risk of infection.

#### Australia

A number of studies involving only a few animals have been undertaken on the role of domestic dogs in the transmission of E. granulosus in Australia (Baldock et al., 1985; Gasser et al., 1990; Grainger and Jenkins, 1996; Jenkins and Andrew, 1993; Thompson et al., 1988). The limited data available suggest that in some rural and urban areas up to 10.2% of domestic dogs are infected. This is likely to be an underestimation of the true prevalence level, as the studies relied upon arecoline purgation and detection of serum antibodies to determine parasite presence. Dogs are infected by ingestion of raw offal from sheep, wild pigs, or macropod marsupials. Classes of dogs found infected include those belonging to recreational pig hunters, suburban residents of Perth, and Aboriginal communities

in New South Wales (Jenkins and Andrew, 1993; Thompson *et al.*, 1988; Thompson *et al.*, 1993). Domestic dogs are rarely treated for intestinal worms.

Between 48% and 93% of wild dogs, consisting of dingoes and dingo/domestic dog hybrids, have been found infected with very heavy *E. granulosus* worm burdens in Queensland (Baldock *et al.*, 1985), Victoria (Grainger and Jenkins, 1996), and New South Wales (Jenkins and Morris, 1991). In addition to a wildlife cycle wild dogs may also be responsible for both sheep and human infection.

#### New Zealand

Fifty years ago approximately 10% of sheepdogs in the rural areas and over 56% of dogs owned by professional rabbit hunters were infected with *E. granulosus* (Sweatman and Williams, 1962). Anational control programme eliminated the parasite and the country now is in a 'maintenance of eradication' phase (see Chapter 14).

#### North America

The cervid strain (*E. canadensis*) is mainly maintained in a wildlife cycle involving wolves as definitive hosts and moose (*Alces alces*) as intermediate hosts. Dogs fed offal from wild ungulates are the most important source of infection for humans (Himsworth *et al.*, 2010; Moro and Schantz, 2006). Wolves translocated from British Columbia and Alberta to Yellowstone National Park were coproantigen tested prior to movement and found to have high rates of *Echinococcus* antigen positivity 75.6% (62/82), most likely the cervid strain. *E. granulosus* has also been recorded in wolves from this area (Foreyt *et al.*, 2009).

*E. granulosus* (sheep strain, senso stricto) was probably introduced to Utah by sheepdogs imported from Australia in 1938 (Crellin *et al.*, 1982). Infection then spread in the western states by movement of infected sheep. Transmission occurs between sheep and the large numbers of dogs used to herd them, which are maintained in a transhumant system employed by the Basque
Americans living in the Central Valley of California, and in native Americans in Utah (Andersen *et al.*, 1983). CE is also found among native Americans who practise home slaughter in Arizona and New Mexico (Schantz, 1977).

#### South and Central America

In Florida, Uruguay, dogs are used for herding sheep. Home slaughter is frequent and in one study in a rural area 13.2% of dogs were found to be infected. Reinfection 2–4 months after treatment was high (Cabrera *et al.*, 1996). Mean worm burden (by arecoline purgation) in Durazno Department (Uruguay) was 67 (range 1–1020) where the prevalence was 20% (Cohen *et al.*, 1998). Feeding of offal to dogs was significantly correlated with *E. granulosus* infections in dogs and CE infection in humans (Carmona *et al.*, 1998).

The prevalence of infection of dogs in Peru is high in the central and southern highlands, ranging from a prevalence rate of 8–46% in Junin and 32–37% in Puno. In urban areas, prevalence rates range from 3.42% in Lima to 48.2% in Arequipa (Moro *et al.*, 1997). Most human infections in Peru are due to infection with the sheep (G1) strain of the parasite (Santivanez *et al.*, 2008).

CE is prevalent throughout Chile (Arambulo, 1997), but is especially common in the south of the country where active control programmes have been in place for many years (see Chapter 14). CE is also common in the high sierra of Bolivia and in the Rio Grande do Sol in Brazil (Moro and Schantz, 2006).

CE infection in Central America is rare and most probably maintained in a pig-dog cycle. In many countries poor abattoir conditions exist, with dogs gaining access to discarded offal (Schwabe, 1984).

#### Diet

The diet available to dogs obviously plays a pivotal role in their becoming infected with *E. granulosus*. In most nomadic or transhumant populations dogs are fed scraps, and scavenge around the temporary encampments. In many instances human faeces comprises an important part of the dogs' diet, and dogs are welcomed for the sanitary role that they play (Watson-Jones and Macpherson, 1988). Food availability varies considerably, even within regions where socio-cultural and socio-economic conditions are similar. For example, in Turkana 63.5% of 263 dogs were found infected in the north-west of the district, while only a few hundred miles east none of 80 dogs owned by Turkanas living along the shores of Lake Turkana were infected (Macpherson et al., 1985). The lakeshore dogs fed almost exclusively on fish scraps, while the dogs in the west fed on livestock that had died during the 1978–1981 drought. In Turkana dogs may scavenge from human cadavers, increasing the role of humans in the life cycle of the parasite there (Macpherson, 1983). There are no abattoirs outside the major towns of Lodwar, Kakuma, Lokitaung, and Lokichoggio, so offal from infected animals that are slaughtered at the temporary nomadic homes are also sources of infection for dogs.

In low-income countries conditions at abattoirs are not always appropriate for control of *E. granulosus* infection in dogs, and dogs are allowed to scavenge from carcasses or from offal that is discarded (Ibrahem and Gusbi, 1997; Irshadullah *et al.*, 1989; Ouhelli *et al.*, 1997; Schwabe, 1984; Wachira *et al.*, 1993). Thus in some countries such as in India, and North and sub-Saharan Africa, urban cycles of *E. granulosus* occur. In Egypt, dogs have been recorded with higher prevalences of *E. granulosus* in areas where abattoirs were present than in areas where they were absent (Moch *et al.*, 1974).

In a number of countries in West Africa and Asia some people eat dogs, which would be hazardous to the people preparing them as well as to the consumers (Schwabe, 1991; Simoons, 1961). In Turkana, jackals and hyenas were consumed during periods of drought, but the people denied ever eating dogs (Macpherson *et al.*, 1983).

On many continents dogs used for herding are at risk from infection when they scavenge from dead livestock, particularly sheep (Schwabe, 1984). In rural Kazakhstan, for example, the shepherd dogs associated with livestock husbandry have a mean prevalence of 23% compared to village dogs kept as pets or for security from the same district, having a prevalence of 5.8% (Torgerson *et al.*, 2003b). Thus ample opportunities for such scavenging occur, particularly in nomadic or transhumant situations where livestock are moved over vast distances. These scavenging opportunities increase the risk for human CE among such peoples (Macpherson, 1995).

#### Socio-economic factors

A number of socio-economic factors operating at the individual, community, and national levels, which vary in different parts of the world, contribute to the transmission of *E. granulosus* including:

- Poverty. Inability to pay for treatment of owned dogs and for diagnosis/treatment of individuals with CE.
- Lack of education on the public health importance of CE in endemic communities, specifically a lack of knowledge about the life cycle of *E. granulosus*. In endemic countries information about the transmission of the parasite and its prevention is rarely taught, outside of specific control activities.
- Lack of veterinary and medical facilities and diagnostic centres.
- Lack of abattoirs. Areas where home slaughter is commonly practised.
- Lack of trained personnel.
- Lack of dog control programmes, resulting in numerous, usually young, stray and/or feral dogs which are allowed to roam.
- Lack of a safe piped water supply. Hygiene in such areas is naturally compromised if water has to be carried over long distances to the home.
- Pastoralists are at greater risk of CE than agriculturists or urban dwellers.
- Transhumant or nomadic pastoralists who live in many parts of the world appear consistently to have the greatest risk of CE.
- Abattoir workers are a high-risk group for CE.

A greater understanding of these factors, and also particular socio-cultural factors, is essential to the successful implementation of control programmes.

## Human and dog behaviour and Echinococcus granulosus transmission

The routes of transfer of eggs from infected dogs to intermediate hosts, including humans, remain arcane. This process must involve a complex mixture of environmental, socio-cultural, and behavioural factors. Dog contact is a major risk factor (Watson-Jones and Macpherson, 1988; Moro et al., 2008; Tiaoying et al., 2005; Yang et al., 2006). One study, which documented the movements of 31 dogs for 24,541 observation-minutes, in areas of high, medium, and low human CE prevalence, found that the amount of time dogs spent in their houses was significantly correlated with an increased prevalence of CE (Spearman's rank correlation coefficient (rs) = +0.986, p<0.01). A significantly positive correlation was also found for homesteads which allowed dogs to defecate in the home area, clean children, and to lick eating utensils (Watson-Jones and Macpherson, 1988). Surprisingly dog contact is not always a risk factor for transmission of CE, especially in climates where eggs may survive in the environment for long periods of time (Carmona et al., 1998; Torgerson et al., 2003b; Bai et al., 2002). There is also some evidence that water or food contamination may be a possible source of infection (Craig et al., 1988; Dowling et al., 2000; Macpherson and Craig, 1991; Macpherson et al., 1989a; Torgerson et al., 2003b). Lack of association with contact may be a consequence of infection occurring many years earlier, and recall is difficult for subjects of epidemiological studies. Also of importance is the fact that in many highly endemic regions dog ownership and dog contact is almost universal, so this factor cannot discriminate between infected and non-infected individuals (Torgerson et al., 2009).

One important risk factor that has been associated with infection with CE is poverty or relatively low income, or unemployment (Budke *et al.*, 2005; Torgerson *et al.*, 2009; Torgerson *et al.*, 2003b).

Transmission from intermediate hosts to dogs is more predictable. Dogs are more likely to become infected if they are young, allowed to roam, fed on raw offal, offal in the community is not disposed of properly, the dogs do not receive anthelmintic treatment, or the dogs' owners are ignorant of the disease (Budke et al., 2005; Buishi et al., 2005, 2006; Macpherson, 2005; Torgerson et al., 2003b; Ziadinov et al., 2008). In one study, questionnaires used during ultrasound screening surveys indicated that, in Morocco, 90% of hydatid cysts from sheep slaughtered at home were fed to dogs (Macpherson et al., 2004). A similar proportion is likely in other endemic regions facilitating hydatid cysts from intermediate hosts to dog transmission.

#### Control and surveillance

There have been a number of island and continental control programmes for *E. granulosus*: these are covered in Chapter 14 and only a brief overview of control measures that are applied to dogs will be considered here. Many control programmes have been implemented and several have been very successful in reducing the annual incidence of CE in humans and sheep, and *E. granulosus* infections in dogs. Iceland and New Zealand have succeeded in eliminating CE.

A number of options are available for control (Chapter 14) but most programmes have had similar strategies to control *E. granulosus* in dogs, which include:

- Education of the local population. An important aspect with any educational programme is compliance with the control approach, for example complying with dog registration and treatment schedules, not feeding cysts to dogs, etc.
- Dog registration.
- Elimination of stray and unwanted dogs.
- Population management of wanted dog populations.
- Prevention of access of dogs to infected offal. This may be achieved through strict rules of disposal of infected offal

in abattoirs and preventing dogs from gaining access to such facilities. In the absence of such facilities, education of those who carry out home slaughter should be implemented.

- Regular dosing of dogs with praziquantel. Some programmes implement an intense dosing schedule every 6 weeks, whereas others examine epidemiological factors and dosing is timed to prevent transmission when the intensity is likely to be highest and the greatest cost:benefit value is obtained. If regular treatment of dogs is the only control method than this clearly must be an intensive treatment schedule It will result in parasite elimination, providing most of the dogs are treated and the programme is continued over a long period of time, usually decades.
- If adequate controls of the intermediate host are implemented, such as slaughter control, then this will potentiate the use of anthelmintics in dogs.
- A new vaccine for use in sheep (EG95) has become available and appears to be highly effective. Vaccinating sheep has a potentially useful role in preventing infection in dogs.
- Options for control will need to be tailored to the availability of local resources and logistical considerations. A detailed description of various options can be found in Torgerson *et al.* (2011).

Surveillance in dogs may be carried out through coproantigen tests which have a good sensitivity and can detect prepatent infections. This technique has been implemented in a number of countries (Acosta-Jamett *et al.*, 2010; Mastin *et al.*, 2011; Pierangeli *et al.*, 2010).

## Echinococcus ortleppi, E. intermedius, and E. canadensis

Until recently these species were considered to be genotypes of *E. granulosus*. Molecular and other evidence now strongly indicate that they should be promoted to species status. Although all these species are zoonotic, they generally cause far fewer cases of human CE than *E. granulosus*. Their impact on human health may be underestimated, as generally hydatid cysts are not routinely genotyped and hence the relative contribution of these species is unknown. Some trends have been recorded and these can be summarized. Human infections with *E. canadensis/ E. intermedius (E. granulosus G6-G10)* have been recorded in Argentina (Soriano *et al.*, 2010), Peru (Moro *et al.*, 2009), Turkey (Snabel *et al.*, 2009), Mongolia (Jabbar *et al.*, 2011), Sudan (Omer *et al.*, 2010), and Central Europe (Schneider *et al.*, 2010). Livestock in these areas are also commonly infected with this genotype of parasite, with goats, pigs, and camels frequently being an important reservoir.

*E. ortleppi* has been seen in humans and livestock in Brazil (de la Rue *et al.*, 2011), in livestock in India (Pednekar *et al.*, 2009), Italy (Casulli *et al.*, 2008), and East Africa (Dinkel *et al.*, 2004).

## Echinococcus multilocularis (Leuckart 1863)

The small (1.2-4.5 mm) adult tapeworms live in the small intestines of wild canids. Throughout most of the parasite's range the red fox (Vulpes vulpes) is the main definitive host. In the northern tundra zone of North America and in northern Russia the arctic fox (Alopex lagopus) is an important definitive host. In central North America between 6% and 35% of coyotes (Canis latrans) have been found infected (Eckert et al., 2011). Other relatively important wild definitive hosts include wolves (C. lupis) and sand fox (Vulpes corsac) which may be commonly infected in Eurasia. Domestic dogs and cats also serve as definitive hosts (see below). Small mammals including microtine and arvicolid rodents, and occasionally other groups such as ochotonidae, are intermediate hosts for Echinococcus multilocularis. In these hosts the parasite develops rapidly, in contrast to the much slower developing metacestode of *E. granulosus*.

#### Distribution

*E. multilocularis* is predominantly maintained in predator:prey wildlife cycles, and in most

endemic areas humans, with their domestic animals, are ecologically separated. The parasite is found over an extensive area of the northern hemisphere, extending from the tundra zone of North America through northern and central Europe and Eurasia, to China and the northern islands of Japan. Its southernmost limits in Asia are northern India, Iran, and eastern Turkey (Eckert *et al.*, 2011; Rausch, 1993). *E. multilocularis* eggs have become adapted to cold climates and can survive temperatures of  $-50^{\circ}$ C. Eggs can thus overwinter and be viable when the intermediate hosts emerge after the winter (Schiller, 1955).

## Dogs as definitive hosts of *Echinococcus multilocularis*

Dogs are susceptible to E. multilocularis and infection occurs when dogs ingest infected intermediate hosts. Huge worm burdens may result in both dogs and foxes. On St Lawrence Island mean infection rates in Arctic foxes was 7400-54,000 (range 1-84,000) (Rausch et al., 1990). In the red fox in urban areas of Zurich infections of over 10,000 worms were found in 8% of the 133 infected foxes (Hoffer et al., 2000). The prepatent period is slightly shorter than for E. granulosus at about 28 days, and proglottids contain only between 200 and 300 eggs. The adult parasites probably live for approximately 3-4 months with maximum egg excretion 6-103 weeks after infection (Kapel et al., 2006). More than 100,000 eggs per gram of faeces may occur.

The suitability of cats as definitive hosts is believed to be poor, with experimental infections in cats resulting in very few viable worms and few eggs being produced (Kapel *et al.*, 2006).

In China dogs have been found to be infected in Gansu (6 out of 58) (Craig *et al.*, 1992) and Sichuan provinces (up to 20%) (Budke *et al.*, 2005). In south Gansu dog ownership per se was not a risk factor for human AE; rather, number of dogs and period of dog ownership were the major risk factors (Craig *et al.*, 2000). In this montane agricultural region a semi-domestic cycle between dogs and microtine rodent species is likely to occur during periods of high population density for susceptible rodent species.

Within Tibetan communities dogs play an important role in the transmission of AE to humans (Vaniscotte *et al.*, 2011). Domestic dogs are also probably involved in semi-domestic transmission of *E. multilocularis* involving the common lagomorph species in this biotype, *Ochotona curzonae*. In both Gansu and Sichuan, higher AE rates in women may be related to closer contact of females with dogs.

In Central Asia dogs have been shown to have a high prevalence of *E. multilocularis* (Ziadinov *et al.,* 2008) and these may prove to be a risk for human AE in Kazakhstan and Kyrgyzstan.

In Japan stray dogs have been found infected on Reubun Island (1.6% of 3224) (Yamashita, 1973) and in 2% of dogs on the island of Hokkaido (Iida, 1969). In both areas the red fox is perceived as the main definitive host.

In North America, *E. multilocularis* is currently an important public health problem only among the Yupik Eskimos in the northern tundra zone of Alaska, despite the parasite's distribution, including as far south as the midwest of the USA (Rausch, 1993; Schantz *et al.*, 1995). The parasite has been found on a number of the subarctic islands, including St Lawrence Island, where in the 1950s 12% of dogs autopsied were infected (Rausch *et al.*, 1990). Dog ownership and tethering dogs near houses was an important risk factor for patients found to have AE (Stehr-Green *et al.*, 1988).

It has been speculated that dogs may have been the route through which the parasite was spread from the northern tundra zone to southern Canada and to central areas of the northern United States, especially North Dakota and northern Manitoba (Rausch, 1993). The parasite has spread from these areas and has now been reported in 11 contiguous states in the United States and in three Canadian provinces (Schantz *et al.*, 1995). So far the parasite in this area has not been found in domestic dogs and only two human AE cases have been confirmed in the last 50 years (Schantz *et al.*, 1995).

In Europe, little is known about the importance of dogs in the transmission of

E. multilocularis to humans as there are few stray dogs and, until recently, the only means of diagnosis was necropsy. Studies which were carried out generally involved small numbers of dogs and salient risk factor assessment was lacking. The recent development of ante-mortem diagnostic tests (see below) has facilitated much larger studies. A recent ELISA coproantigen study with confirmation by PCR of 660 dogs in Switzerland found a prevalence of 0.3% (Deplazes et al., 1999). In Austria, cat ownership and hunting in the forest were found to be important risk factors, whereas dog ownership was not (Kreidl et al., 1998). In Austria, as elsewhere in Europe, dogs are mostly pets and not used for hunting. In Germany, 43 of 17,894 (0.24%) canine faecal samples were PCR-positive for E. multilocularis (Dyachenko et al., 2008). The samples originated from all regions of Germany and confirmed that canine infection with E. multilocularis in Central Europe occurs, albeit at a low frequency.

In an attempt to estimate the relative capacities of foxes, dogs, and cats to contaminate the environment with E. multilocularis eggs, a model calculation was carried out for the Canton of Zurich, Switzerland (Eckert and Deplazes, 1999). The population size and prevalence of E. multilocularis in the three definitive host species was calculated. Foxes were the largest group of E. multilocularis carriers, whereas the numbers of infected dogs and cats were much smaller and represented only 7% and 16% of the number of infected definitive hosts, respectively. Apparently, in this epidemiological situation, foxes were the main contaminators of the environment with E. multilocularis eggs. Such calculations can provide a few suggestions for the importance of the various definitive hosts, but they are woefully incomplete, as many other factors play a role. For example, although the prevalence rate in dogs and cats was small, they have a closer contact with humans than foxes, providing greater opportunities for being the source of human infection. Cats have now been shown, at least experimentally, to be very poor hosts of E. multilocularis with very few worms establishing and no viable eggs production (Deplazes et al., 2011; Kapel et al., 2006) so the epidemiological significance of cats in

transmission is likely to be insignificant. On the other hand, it has been noted recently that fox populations are increasing in the cities of Europe, and in Zurich, Switzerland, it has been estimated that there are between 300 and 400 foxes within the city limits, with 47% being infected with E. multilocularis (Hoffer et al., 2000). It is known that such foxes visit public parks and swimming pools (Deplazes et al., 1999). There is now a statistically significant increase in the numbers of human AE cases in Switzerland, which is temporally correlated (with a lag of 10–15 years) with the increase in the fox population (Schweiger et al., 2007). This association with the increase in fox population does not prove that foxes transmit to humans in Europe. What it does demonstrate is that the increased E. multilocularis biomass now present is leading to greater numbers of cases. The conduit to humans may be contact with foxes (as previously discussed) or there may now be greater opportunities for dogs to become infected. It should also be noted that dogs are often coprophagous and will eat fox faeces, (possibly resulting in the sporadic cases of hepatic AE being recorded in dogs (Staebler et al., 2006) and egg passage may put owners at risk. Even more likely is the habit of dogs rolling in fox faeces, and the fur being contaminated with eggs, which could permit transmission.

The introduction of new diagnostic tests may not only be used for ante-mortem diagnosis of dogs and cats, but also potentially be able to detect *E. multilocularis* infections in faecal samples collected in the field. This will facilitate studies on environmental contamination, to examine the relative contribution of dogs and cats compared to that made by foxes, and enable studies to be carried out to examine potential routes of infection for humans.

## Diagnosis of Echinococcus multilocularis in dogs

Until recently the only means of accurately diagnosing *E. multilocularis* infections in dogs was by autopsy and the subsequent morphological identification of the adult

worms. The development of ELISA and PCR tests for screening faeces for coproantigens or worm DNA has revolutionized diagnosis of not only patent but also prepatent infections in definitive hosts (Deplazes *et al.*, 1999; Dinkel *et al.*, 1998). The coproantigen test has a sensitivity of 80% and a specificity of 95–99.5%. Confirmation of infection may be made using PCR to detect *E. multilocularis* DNA, which increases the sensitivity to 94% and has a specificity of 100% (Deplazes and Eckert, 1996; Dinkel *et al.*, 2011; Torgerson and Deplazes, 2009).

## Treatment of *Echinococcus multilocularis* in dogs

The treatment of choice is praziquantel. As with *E. granulosus* no resistance to the drug has yet been reported, and the drug is effective in a single dose.

## Epidemiology and public health importance

Foxes infected with *E. multilocularis* have traditionally been considered to be an important health hazard to fox hunters, however there is no direct evidence for this. When hunters in the United States and Japan were screened by serological tests no increased risk of seropositivity was observed (Schantz *et al.*, 1995).

Indirect contact with an environment contaminated by fox faeces, such as wild fruits and/or herbs has been considered an important mode of infection, though detailed studies are lacking. Dog (or cat) ownership over a reasonable period (years) within endemic areas is possibly a greater risk factor for human AE (see above), together with an agricultural occupation or background, and households close to a landscape or biotype capable of sustaining susceptible intermediate host populations (Bresson-Hadni *et al.*, 1994; Craig *et al.*, 2000). Infected dogs, rather than wild canids, may pose the greatest risk for human AE infection (Vaniscotte *et al.*, 2011).

## Control and surveillance

The only example of elimination of *E. multi-locularis* occurred on Reubun Island (Japan) 30 years after the parasite had been introduced inadvertently with translocated red foxes in 1924–26. Approximately 1% of the population (129 AE cases) was infected, 19% of red foxes and 1.6% of dogs. A 5-year fox and dog culling control programme appeared to eliminate the parasite by 1995 (Craig *et al.*, 1996; Yamashita, 1973).

There has been a single trial to treat dogs as part of a control programme for *E. multilocularis*. This took place in St Lawrence Island, where dogs were treated monthly with praziquantel over a 10-year period. This reduced the infection in the rodent intermediate hosts from 29% to 5%. The prevalence rate in the intermediate hosts, however, rebounded to the original rates soon after dosing of dogs was discontinued (Schantz *et al.*, 1995).

In southern Germany a trial to reduce the prevalence of E. multilocularis in foxes (Vulpes *vulpes*) demonstrated that after six treatments the prevalence of the parasite in these definitive hosts fell from 32% to 4% (Schelling et al., 1997). Likewise, in the city of Zurich, regular treatment of foxes using praziquantel baits has been shown to decrease the prevalence substantially (Hegglin et al., 2003), with monthly baiting of foxes appearing to be the most effective strategy (Hegglin and Deplazes, 2008). Similar results have also be found with intensive baiting strategies in Germany (Konig et al., 2008). It has been proposed that only those dogs and cats at risk of infection through eating wild-caught intermediate hosts should be treated regularly with praziquantel (Eckert and Deplazes, 1999). The possibility of introducing a dog-screening programme with ELISA tests to detect coproantigens provides an exciting new approach to E. multilocularis epidemiology and surveillance.

## *Echinococcus vogeli* (Rausch and Bernstein, 1972)

*Echinococcus vogeli* has a restricted global distribution and has only been reported within the range of its wild definitive and intermediate hosts in Central and South America: in Costa Rica, Panama, Colombia, Ecuador, Venezuela, Brazil, and Bolivia (Rausch, 1993). The disease in humans who serve as accidental intermediate hosts is known as polycystic echinococcosis (PE), or hydatid disease. The adult parasites were first described from specimens recovered from the small intestine of the bush dog, Speothos venaticus (Rausch and Bernstein, 1972), which is the only known wild definitive host species of this parasite. The animal had been captured in its natural habitat in Esmeraldas Province, Ecuador, and kept in the Los Angeles Zoo. The bush dog was responsible for infecting five different species of non-human primates housed in nearby cages, and most of them subsequently died of PE (Howard and Gendron, 1980). There were no human cases, but this incidence does highlight how infective the eggs are for non-human primates.

The paca *Cuniculus paca* serves as the main intermediate host. Agoutis (Dasyprocta spp.) and spiny rats (Proechimys spp.) have also been found to harbour E. vogeli protoscoleces (Rausch et al., 1981). Domestic dogs can also serve as definitive hosts, and experimental infections of dogs with cysts from an agouti were confirmed as being E. vogeli (Rausch et al., 1984). In its natural habitat *E. vogeli* is maintained in a predator:prey cycle. As Speothos spp. hunt in packs, many bush dogs may be infected from a single paca kill. The risk of human infection from wild definitive hosts would be rare, since bush dogs are secretive and very wary of humans, and move further into the forest when humans encroach on their territory. Contact rarely occurs. In endemic areas, dogs are used to hunt and are commonly fed viscera from pacas, so that human infections are probably acquired from the faeces of infected dogs. Feeding dogs with paca offal is an important risk factor and in Colombia a hunter's dog has been found to have the adult parasites (D'Alessandro and Rausch, 2008). In Brazil, Meneghelli et al. (1990) found that all seven patients with polycystic hydatid disease had contact with dogs that had been fed offal from pacas.

On radiological examination, the disease in humans gives the appearance of multiple cysts of E. granulosus (Meneghelli et al., 1992b). Cysts are usually located in the liver but also infect the lungs, spleen, pancreas, peritoneal cavity, and mesentery (D'Alessandro and Rausch, 2008; Meneghelli et al., 1992b). Differentiation between E. vogeli and E. granulosus is possible using protoscolex hook morphology, PCR, and ELISA. Human infections have been reported in most countries within its known range in neotropical America (Meneghelli et al., 1992b; Nunez et al., 1993; Rausch, 1993). In Ecuador at least 12 human cases have been diagnosed from diverse geographic regions, including the coastal plain, Amazon basin, and Andean plateau (Nunez et al., 1993). In Brazil, most cases have been reported from the Amazon region, but a few came from the state of Sao Paulo (Meneghelli et al., 1992b).

Albendazole given over a period of several months successfully treated four of six patients (Meneghelli *et al.*, 1986, 1992a). The remaining two patients had some remission of the disease. It would be impossible to control the parasite in its natural habitat, but making hunters aware of the dangers of feeding offal from pacas to their dogs would help decrease human exposure in endemic regions. Regular treatment with praziquantel of dogs that are fed such offal would also be advisable.

## Diphyllobothriosis

Within the group of tapeworms belonging to the genus *Diphyllobothrium*, *D. latum* is the predominant of 14 recognized species with regard to numbers of human infections, which amount to approximately 9–20 million (Lloyd, 2011). *D. latum*, known as the 'broad' tapeworm, as the proglottids are usually wider than they are long, is the largest tapeworm of humans, growing to a length of 3–25 m and a width of 1–2 cm. The parasite is especially prevalent in countries where fish is a major source of protein and is often eaten raw or only partially cooked (i.e. smoked). Offal from the fish is often available to domestic animals and cats, pigs, and especially dogs may serve as definitive hosts. In some areas infection levels in dogs reach 34–47% and they probably serve as the main definitive hosts (Witenburg, 1964). Foci of infection stretch east from France, northern Italy, and the Baltic States, through northern Russia into China, Japan, and North America; and also through South America, including Patagonia, Argentina, Chile, and Peru. Sporadic infections are described in other countries such as Brazil, Cuba, Korea, and Australia, and 1% prevalence was recently described in 6-10-year old children in Karnataka, India. Genetic analyses are required to confirm *D. latum* at all its reported locations (Lloyd, 2011). Marine diphyllobothrosis occurs in marine mammals (seals). Occasionally humans who eat raw or undercooked marine fish, especially anadromous species such as salmonids (Scholz et al., 2009), are also infected. Although human infections have been recorded in Peru, Chile, and Japan, the susceptibility of dogs in these countries is unknown (Miyazaki, 1991).

The life cycle of *Diphyllobothrium* spp. includes copepods as first intermediate hosts (procercoid stage) and freshwater fish as second intermediate hosts (plerocercoid stage) (Rahkonen and Valtonen, 1997). Following ingestion by definitive hosts, such as humans and a range of other fisheating carnivores, and in particular domestic animals such as dogs, cats, and pigs (see above), the plerocercoid larvae mature to adult tapeworms that may contain up to 3000 proglottids. Experimental infections in dogs have shown that egg production starts about 21 days after infection (Wardle and Green, 1941).

Intestinal infection with *D. latum* is usually asymptomatic. In some cases, mild gastrointestinal obstruction, rarely diarrhoea and abdominal pain, and occasionally leukocytosis with eosinophilia, are present. Perhaps the most serious clinical manifestation is the onset of pernicious anaemia, which occurs in approximately 2% of the patients, as shown in studies performed in Finland. This is caused by the extensive absorption of vitamin B12 by the adult tapeworm (von Bonsdorff, 1977).

Prevention and control measures include appropriate cooking of fish and

treatment of infected individuals and domestic animals, particularly dogs, with praziquantel. Regular treatment of domestic carnivores with praziquantel, especially those being fed raw fish, can dramatically reduce environmental contamination of natural water resources with parasite eggs, and thus reduce transmission. Preventing access of wild carnivores to aquaculture facilities by appropriate fencing also helps control the parasite in such areas.

## Cestode Species of Minor Zoonotic Importance

#### Dipylidium caninum

Dipylidium caninum is one of the commonest tapeworms of dogs and cats in most parts of the world (Boreham and Boreham, 1990). It is especially common in neglected dog populations which have large ectoparasite populations. Although prevalent worldwide in pets, human infection is uncommon (<200 reports) but underestimated. In the United States 43 cases were reported in a 5-year period when drug use could be recorded. Infection occurs usually in children under 6-12 months of age (Lloyd, 2011). Children also serve as definitive hosts, and adults only rarely (Moore, 1962); this is probably due to increased opportunities for children to become infected. The adult parasite lives in the small intestine and rarely exceeds 50 cm in length. Proglottids migrate out of the anus or are shed in faeces and are easily identifiable as they resemble a large rice grain and are either passed singly or as a short ribbon of up to 10 proglottids. A hand-lens inspection of freshly passed proglottids reveals the lateral genital pores and egg packets, which can be used to differentiate this parasite from the taeniids. Each D. caninum proglottid contains up to 20 egg packets, each containing 6-12 infective eggs. Fleas (Ctenocephalides felis and C. canis) and the dog louse (Trichodectes canis) serve as intermediate hosts. Biting lice can ingest oncospheres at any stage in their life cycle, as all stages have chewing mouth parts, but fleas are only infected in the larval

stage as the adults have piercing mouth parts. Development in the obligate ectoparasite, the louse, takes up to 30 days, while in the flea larvae in the environment may take up to a couple of months, depending on the ambient temperature. The cysticercoid in the louse or flea is ingested by the definitive hosts and the prepatent period is about 3 weeks.

The adults, which may number several hundred, are not pathogenic. Proglottids passing out of the anus may cause mild pruritus.

Treatment of children, dogs, and cats is with praziquantel, niclosamide, or nitroscanate. Control of the ectoparasite intermediate hosts should be carried out simultaneously. Special attention should be paid to the sleeping area of domestic dogs and cats.

#### Taenia spp.

There are at least three taeniid species, *T. multiceps, T. serialis,* and *T. brauni,* which have dogs and other canids as definitive hosts; a few humans have been identified to be infected with the larval stage. In addition, *T. solium* cysticercosis has been recorded in dogs.

Taenia multiceps (syn. Multiceps multiceps)

The parasite is regarded as being common in dogs in Australia, Europe, South America, and Africa but has disappeared from New Zealand and the United States. A prevalence of 26.6% of dogs in Wales has been reported (Hackett and Walters, 1980). The prepatent period in dogs is between 38 and 43 days (Willis and Herbert, 1987). Adult worms grow up to about 100 cm and proglottids are shed in the faeces. Intermediate host species include wild ruminants, chamois, cattle, goats, and - most importantly - sheep. Ingested eggs hatch in the small intestine and the oncosphere penetrates the gut and lodges primarily in the CNS, especially the brain. Here, over a period of about 8 months, it develops into a coenurus (Cysticercus cerebralis), giving

rise to many hundreds of daughter protoscoleces, hence multiple worm infections are common in dogs. Clinical manifestations depend on the location of the cyst and may include circling, paraplegia, and peculiarities in gait known as 'gid'. A few hundred cases in humans have been reported globally (Lloyd, 2011).

#### Taenia serialis and T. brauni

Intermediate hosts include lagomorphs and rarely rodents. Cysts are usually located intramuscularly or subcutaneously. Protoscoleces align in rows or series in such cysts, hence the name *C. serialis*. Differential diagnosis with *T. multiceps* may be difficult in both adult and cystic stages (for human infections).

Intermediate hosts of *T. brauni* are rodents. Most human infections are subcutaneous or intraocular, and most have been reported from Africa (Lloyd, 2011).

## Spirometra spp.

Adult *Spirometra* spp. are found in dogs, cats, and a range of wild carnivores in many parts of the world, particularly eastern Asia, but also in Africa, North and South America, and Australia. The life cycle of these tapeworms is similar to that of *D. latum* and two intermediate hosts are normally required. The procercoids are found in crustaceans and the plerocercoids in a range of intermediate host species including amphibians, birds, snakes, mammals, and humans (Smyth and Heath, 1970). Humans can be infected in three different ways:

**1.** By ingesting procercoids in crustaceans (*Cyclops* spp.) in drinking water.

**2.** Through ingesting plerocercoids in undercooked amphibia, snakes, birds, and mammals such as pigs.

**3.** By applying poultices (such as split frogs) to skin wounds and especially to the eyes (Lloyd, 2011).

In the latter case plerocercoids migrate from the poultice into the local tissue. This mode of transmission is most commonly found in China and South-East Asia. Plerocercoids can grow up to 30–40 cm. The disease is known as sparganosis (Sparganum was the old name for the plerocercoid stage). Ingested procercoids or plerocercoids penetrate the intestinal mucosa, wander through tissues and may end up in subcutaneous sites where they may encyst. They may cause oedema and inflammation of the periorbital area, the predilection site of the plerocercoids.

There are many different species of *Spirometra* but the dog is the known definitive host of *S. mansoni*, the dominant species in Asia and South America; snakes serve as intermediate hosts for this species. In lions examined in the Serengeti National Park (Tanzania), *Spirometra* was the commonest intestinal helminth recorded (Muller-Graf *et al.*, 1999).

Rarely the parasite proliferates, producing a large number of plerocercoids, which may be fatal (Mueller, 1974). Diagnosis is by finding the plerocercoid, often incidentally when a biopsy of a lump is made. Treatment is by surgically removing the plerocercoid and occasionally praziquantel may be used, especially in heavy or cerebral infections.

## Mesocestoides lineatus

Dogs can serve as both secondary intermediate as well as definitive hosts for Mesocestoides *lineatus*. The parasite has a wide distribution in Asia, Europe, and Africa. Adult worms have been recorded in humans in Japan, China, and Korea (Lloyd, 2011; Miyazaki, 1991). A total of perhaps 30 human cases have been documented (Lloyd, 2011). Mites serve as the first intermediate hosts and have the cysticercoid stage. Dogs and other carnivores, amphibia, reptiles, and birds serve as secondary intermediate hosts with the tetrathyridia stage. The tetrathyridia can multiply asexually in the peritoneum or may develop into adults. The scolex has no hooks. Clinical symptoms include severe diarrhoea, abdominal pain, hunger, and dizziness. In Japan, human infection probably occurs as a result of eating/taking uncooked blood or organs of snakes and turtles as tonics (Miyazaki, 1991).

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# 9 Dogs and Nematode Zoonoses

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Dogs in all parts of the world are very frequently infected with nematodes, which are also known as roundworms. The large ascarid gutworm Toxocara canis is common, especially in young animals, because of its efficient vertical transmission mechanism. Larvae of this species migrate through human tissues when eggs are ingested, causing a variety of clinical and subclinical syndromes. T. canis dominates public health attention among the nematodes of dogs, and is the main reason for preventative chemical deworming of dogs in temperate areas not endemic for the heartworm Dirofilaria immitis. Where heartworm is a major threat to canine health, routine anthelmintic treatment would be expected to strongly suppress T. canis populations. However, in spite of decades of efforts to reduce T. canis transmission to humans through treatment of dogs and public hygiene measures, this species remains very common and human disease continues to occur. This chapter therefore focuses mainly on the control of toxocarosis in dogs in the interests of public health, and reviews the successes and limitations of current strategies. T. canis also serves as a model for other nematode zoonoses. Thus, hookworms have a similar life cycle to Toxocara spp., and measures to prevent environmental contamination

with ascarid eggs should also reduce the threat from hookworm larvae. Other important nematode zoonoses of dogs are briefly reviewed, chief among them *Strongyloides stercoralis*, *Gnathostoma* spp. and *Thelazia callipaeda*. Several other nematode species can infect dogs and humans, but dogs are rarely if ever the main source of infection. This category is not considered.

## Toxocarosis

Toxocarosis in humans can, in principle, be caused by any species of Toxocara. Most attention has traditionally focused on T. canis, but there are good reasons to consider T. cati in cats as an important contributor to environmental contamination with Toxocara eggs, and a potential cause of cases of toxocarosis in humans (Fisher, 2003). T. canis populations in foxes also contribute to environmental contamination with eggs, since prevalence in foxes is typically high. However, in most areas inhabited by humans, dogs greatly outnumber wild foxes, and share the human environment more closely. It is therefore generally considered that T. canis infection in dogs is the main source of toxocarosis in humans (Mizgajska, 2001).

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## Mode of transmission

Adults of T. canis live in the small intestine, where they do not attach to the mucosa but rather maintain position by moving against gut peristalsis. They feed on intestinal contents and generally cause few problems to the host. Males and females mate and the females produce eggs that pass out in the faeces (Fig. 9.1). Very large numbers of eggs are produced (Glickman and Schantz, 1981). Thereafter, the life cycle can be complex (Overgaauw, 1997). The eggs must first develop to the larvated stage before they are infective (Kasai, 1995; Brunaska and Dubinsky, 1995). This occurs at temperatures above around 11°C with adequate moisture (Azam et al., 2012). Infection occurs when mature eggs are ingested and the larvae hatch out and penetrate the intestinal wall. In fully susceptible dogs, these larvae then move via the liver and the lungs, before being coughed up and swallowed, to complete development to the adult stage in the intestine. This process is known as hepatotracheal migration. In older dogs that have previously encountered infection, hepatotracheal migration is rarely completed. Instead, the larvae migrate more widely through the body, and can invade a variety of tissues. By entering an arrested state, larvae can survive in the somatic tissues for many years, perhaps even the lifespan of the host. In female hosts that reproduce, larvae re-emerge from somatic arrest, and cross the placenta and the

mammary glands. Most pups are therefore infected before birth, and continue to ingest larvae throughout the suckling period. Vertical transmission is highly efficient, such that the majority of pups even in well-cared-for pet dog populations are infected (Sprent, 1958; Parsons, 1987; Schantz and Stehr-Green, 1988).

Humans are infected primarily by ingesting larvated eggs. Larvae are sometimes found in the tissue of food animals, which can therefore act as paratenic hosts (Glickman and Schantz, 1981; Stürchler et al., 1990; Yoshikawa et al., 2008). Indeed, seroprevalence has been found to be as high as 47% in adult sheep (Lloyd, 2006). However, it is not known to what extent meatborne infection contributes to human toxocarosis. Eggs are thick-shelled and highly resistant to normal environmental conditions (Azam et al., 2012), and can therefore persist for months or possibly years in soil. Eggs are therefore available and infective long after faeces have degraded, and can be ingested inadvertently following soiling of hands. Serological studies in humans have found evidence of exposure in a wide range of social and age groups, with positive association of risk with rural location, occupations that involve contact with land, and behaviours such as pica (geophagy) in children (Mizgajska, 2001). Traditionally, it was thought that transmission by direct contact with dogs was unlikely, given that eggs require days or weeks to develop to the infective stage. However, larvated eggs have been found on



Fig. 9.1. Egg of Toxocara canis. Approximately 80 µm in diameter UE = Unembryonated; L = Larvated.

the hair of dogs (Wolfe and Wright, 2003), and development to the infective stage while on dog hair has been demonstrated in the laboratory (Keegan, 2011). The potential for infection of humans following handling of dogs therefore exists. Most studies finding substantial numbers of eggs on dog hair have focused on stray dogs or those in poor hygienic conditions, in which contamination of hair with eggs in the environment is highly probable (Roddie et al., 2008). More recent work in well-cared-for pet dogs has found very low levels of eggs on hair (Keegan and Holland, 2010). Moreover, serological studies indicate an inconsistent or weak relationship between dog ownership and antibody titre, which might be expected to be stronger if direct contact were a major route of infection (Won et al., 2008; Rubinsky-Elefant et al., 2010). Therefore, the available evidence continues to point strongly towards general environmental contamination with Toxocara canis eggs, and ingestion through poor hygiene, as the main mode of transmission to humans (Mizgajska, 2001).

#### **Disease in animals**

Disease in adult dogs is rare and mild, and may include digestive disturbance and weight loss, whereas the consequences of infection in young pups can be more severe, and include weakness, emaciation, hypoproteinaemia, ascites, pneumonia, diarrhoea, constipation, and intestinal rupture (Parsons, 1987). Vertical transmission via the placenta and milk is efficient, and large burdens can accumulate in pups as young as 2–3 weeks of age, leading to disease and possibly death. Patent infection, whether associated with disease or not, can be easily diagnosed by faecal flotation, with the characteristic eggs easily recognizable (Fig. 9.1).

## Disease in humans

*Toxocara* ova hatch in the intestine following ingestion of mature, larvated eggs, and the larvae then migrate to the somatic tissues, where they can live for many years (Smith

*et al.*, 2009). Various organs can be invaded, including the viscera, brain, and eyes (Sprent, 1958). Clinical consequences depend on the site of infection, possibly the level and duration of infection, and other unknown factors. Syndromes associated with *Toxocara* infection are grouped into visceral and ocular larval migrans, and covert toxocarosis, with other diverse clinical syndromes also described (Rubinsky-Elefant *et al.*, 2010).

#### Visceral larva migrans (VLM)

Migration of a large number of larvae through the liver and viscera can cause a pronounced inflammatory reaction, and give rise to signs including abdominal pain, fever, malaise, and respiratory signs including coughing and wheezing (Despommier, 2003; Overgaauw and van Knapen, 2008). Infection is often associated with eosinophilia and a rising antibody titre (Smith et al., 2009). However, clinical signs can be vague and with background population seroprevalence often high, diagnosis on the basis of consistent clinical signs and detection of antibodies is insufficient. Since infections do not mature, eggs are not found in the faeces, and unless parasite material is recovered from biopsy material or post-mortem examination, definitive diagnosis is elusive. Larvae can be killed by anthelmintic therapy, but inflammatory reactions can persist and clinical signs can take some time to resolve. The signs and severity of VLM are likely to be a function of the level of infection and host factors.

## Ocular larva migrans (OLM)

Larval migration to the retina is associated with granuloma formation, with various degrees of unilateral visual impairment, including blindness, depending on the location of the larva. OLM can occur in children and adults. Since OLM can involve only a single larva, it is possible that this syndrome can arise from low levels of infection.

#### Other syndromes

Other, less well-defined symptoms have been associated with *Toxocara* infection in humans, including asthma, epilepsy, sleep disturbance,

eczema, and coughing (Overgaauw and van Knapen, 2008). In most cases the causative role of Toxocara is suspected but has not been established. Thus, previous exposure to Toxocara infection has been associated with diminished lung function in cross-sectional epidemiological studies in North America (Walsh, 2010), but the mechanistic relationship between infection, immunology, and lung function has not been investigated. Similarly, Toxocara seroprevalence was higher in patients in Italy who had epilepsy than in matched controls (Nicoletti et al., 2008), suggesting that infection increases the risk of epilepsy, but again evidence does not currently extend beyond statistical association. Studies in rodent models suggest that altered host behaviour might be a feature of larval migration to the brain (Holland and Cox, 2001). It seems likely that larval migration through various tissues and associated inflammation could cause a wide spectrum of clinical consequences. This includes common toxocarosis (Glickman et al., 1987) and covert toxocarosis (Taylor et al., 1987), which were described in different populations but are probably part of the same syndrome. Both refer to relatively low grade symptoms including weakness, recurrent abdominal pain, cough, pruritis, and headache, with or without eosinophilia. Asymptomatic infection is also likely to be common, given high seroprevalence in the absence of widely reported disease.

## **Epidemiology and control**

Although humans of all ages are susceptible to toxocarosis, children are perhaps most likely to be exposed, through poor hygiene after playing in contaminated environments (Gawor *et al.*, 2008; Magnaval *et al.*, 2001). Pica, the consumption of soil and other inappropriate material, can be common in children and is a recognized risk factor for toxocarosis (Schantz *et al.*, 1980). Seroprevalence typically increases with age, as a result of accumulated exposure and long antibody persistence times (Smith *et al.*, 2009).

Control of toxocarosis in humans relies on measures to reduce egg shedding by dogs into the environment, through regular treatment of pets with anthelmintic drugs, control of stray dogs, and encouraging dog owners to remove faeces from public areas. Since prevalence and egg output are highest in young pups, treatment of this group should be early, intensive, and sustained, with most recommended regimes commencing deworming at 2 weeks of age and continuing every 2–3 weeks until 12 weeks of age. At this time, the frequency of treatment can be reduced, though life-long worming of dogs is the only way to ensure that egg shedding continues to be suppressed. Bitches should be wormed at the same time as their pups, since egg excretion increases after pregnancy. Measures to reduce dog fouling are widely conducted, in order to reduce pollution and its aesthetic consequences as well as to reduce Toxocara transmission, but their efficacy has in no case been determined (Atenstaedt and Jones, 2011). Transmission to humans can in principle be reduced by decreasing opportunities for faecal contamination of areas most closely contacted by people, such as children's playgrounds, from which dogs are typically excluded for safety as well as for public health reasons. However, even these measures are not always effective, with some surveys failing to find lower egg density inside such restricted areas than outside them (Kirchheimer and Jacobs, 2008).

Although larvae can be killed by anthelmintic treatment during migration in the pregnant and lactating bitch, drug treatment will not eliminate the reservoir of somatically arrested larvae. Therefore regular treatment of bitches in late pregnancy, or treatment with a persistent anthelmintic, is needed to reduce larval establishment in pups. The rate of application of such treatment by dog breeders can be low, and it must be assumed that most pups will develop patent infections soon after birth, and hence should be treated accordingly.

## Toxascariosis

*Toxascaris leonina* occurs in the small intestine of the dog, cat, and various wild canids and felids throughout the world. Prevalence is typically lower than for *Toxocara* spp. The zoonotic potential of *Toxascaris* is traditionally considered to be limited, because somatic migration in the definitive host does not occur as part of the normal life cycle, and larvae are not vertically transmitted. However, specific studies are not available to confirm the lack of zoonotic threat from this genus. In the dog, intestinal burdens are typically low, and clinical signs are not observed. Measures to reduce *Toxocara* infection in dogs, and contamination of the human environment with eggs, are also likely to be effective in reducing human exposure to *Toxascaris*.

## Hookworms (Ancylostomatosis)

Dogs are host to two genera of hookworm, *Ancylostoma* and *Uncinaria*. Their distribution is unequal, with *Uncinaria* most common in cooler temperate regions, and *Ancylostoma* more prevalent in warmer, sub-tropical and tropical regions (Thompson and Conlan, 2011).

## Mode of transmission

*Ancylostoma* species lay eggs, which pass out in the faeces, and from which larvae hatch and develop in the external environment to the infective third larvae stage (L3). Dogs can be infected by ingesting L3, or L3 can penetrate the skin, and migrate to their final site in the gut via the lungs. In addition, larvae can arrest in the somatic tissues and migrate to the unborn pups, in a similar way to *Toxocara*. *Uncinaria* lacks the percutaneous infection route.

## Disease in dogs

Hookworms are blood feeders and their presence can cause significant disease. *Uncinaria* is typically present at fairly low levels and, except in working dogs (such as racing greyhounds) kept in external runs that allow the build-up of large numbers of larvae, infection does not usually cause clinical signs beyond transient diarrhoea. *Ancylostoma* spp., on the other hand, often causes significant disease. Percutaneous infection is associated with erythema and inflammation of the skin of the feet, especially the interdigital area, and can cause lameness. Accumulation of large burdens of adult worms, especially in pups, can cause severe anaemia and haemorrhagic diarrhoea. *A. caninum* is the most widespread and common species in dogs, with *A. braziliense* more restricted in distribution and apparently less pathogenic in dogs. Infection in dogs can be diagnosed by flotation and identification of the egg.

### **Disease in humans**

The larvae of some species of Ancylostoma, especially A. braziliense, can penetrate the skin of humans, causing cutaneous larva migrans (CLM), while others such as A. caninum have been implicated in eosinophilic enteritis, neuro-retinitis, and other manifestations in humans (Bowman et al., 2010). CLM occurs when L3 penetrate the skin and migrate within the dermis. Although this infection does not mature and is often limited to the skin, the inflammatory reaction can be considerable, leading to pruritis and pain in association with the development of erythematous tracts as the larvae migrate. Usually the infection is self-limiting and can last days, weeks, or even months. After elimination of the larvae, scarring can be considerable. CLM is most common in warm, moist areas in which humans walk barefoot, and disease is most common in the tropics and sub-tropics, especially in children.

## Methods of control

Control strategies are similar to those for *Toxocara*, with regular anthelmintic treatment of dogs, and environmental hygiene – especially faecal removal and disposal – forming the mainstays. In dogs housed together in runs, larval levels can build up considerably, and moving dogs between runs might be necessary, along with regular treatment. Burdens

can sometimes be difficult to clear even with repeated treatment, possibly due to continued larval release from the somatic reservoir (Georgi and Georgi, 1990). Normal hygiene precautions can reduce human exposure, as well as limiting skin-to-ground contact, for example by wearing shoes.

## **Filariosis**

Filarial nematodes generally occupy the connective tissues, and are transmitted by arthropod ectoparasites. Genera of zoonotic importance that infect dogs include *Dirofilaria* and *Brugia*.

## Dirofilaria immitis

This species causes heartworm disease in domestic dogs. The adult worms are large and live in the right side of the heart, causing congestive heart failure as well as a range of other complex clinical syndromes including coagulation disorders. Microfilariae are released into the blood and infect the mosquito vector during feeding, where they mature to the infective L3 stage, to be reinjected during subsequent feeding. The adult worms take many months to mature and can live for several years. D. immitis is traditionally distributed in warmer climates, but has spread in recent years as a result of climate change and dog movement (Genchi et al., 2008). Humans can be infected, but such infections are very rare. Worms can migrate to the lungs and sometimes to the subcutaneous tissues, but do not mature and cause no significant pathology. Serology, radiography, and biopsy can be informative.

#### Dirofilaria repens

The adults of this species occupy the subcutaneous tissues of dogs and other carnivores in Europe, Asia, and Africa. Transmission to humans via infected mosquitoes leads to larval migration and maturation, especially in subcutaneous tissues, but also in the subconjunctiva. The most common manifestation is a painful, erythematous nodule 1–6 cm in diameter. The infection does not progress beyond this stage, but surgical excision might be performed. In theory, spread of *D. repens* northwards in Europe places more dogs and humans at risk of disease (Genchi *et al.*, 2010). Treatment of dogs can be achieved using arsenical drugs and macrocyclic lactones (Baneth *et al.*, 2002). However, most infections in dogs appear to be subclinical, forming a reservoir of zoonotic disease.

### Brugia malayi

*B. malayi* causes lymphangitis and related clinical disease in humans in tropical South-East Asia. Although the infection has been reported in dogs, the main animal reservoirs are monkeys and cats, and the infection also circulates between humans (Meyrowitsch *et al.*, 1998). Dogs are not considered to be a source of zoonotic disease.

## Gnathostomosis

Gnathostoma spinigerum is found in gastric nodules in dogs and wild carnivores, including canids and felids. Eggs are shed in the faeces and pass through an aquatic copepod intermediate host and a range of paratenic hosts including freshwater fish, amphibians, reptiles, small mammals, and poultry (Nuamtanong et al., 1998). In dogs, larvae undergo a destructive migration through the abdominal cavity and liver before reaching the stomach, where they develop in the mucosa, producing protruding gastric tumours. Dogs can be asymptomatic or suffer from vomiting and polydipsia. Diagnosis is by identification of eggs in the faeces, and worms are killed by anthelmintic therapy. Humans become infected by consumption of meat from infected paratenic hosts containing encysted L3 stage larvae. Larvae do not mature in the stomach, but rather migrate to the skin, most commonly forming erythematous, pruritic swellings (Ruznak and Lucey, 1993). Deeper migration involving the respiratory tract and

other organs can occur, leading to more severe disease, which in the case of CNS migration can be fatal (Schmutzhard *et al.*, 1988). Diagnosis is by recovery of worms by biopsy, and/or serology (Nopparatana *et al.*, 1991; Maleewong *et al.*, 1991). Anthelmintic treatment is effective. Prevention is based on avoiding consumption of poorly cooked paratenic hosts, especially freshwater species, in endemic areas.

## Thelaziosis

Thelazia californiensis and T. callipaeda infect dogs and cats in North America and in Asia, respectively, with recent emergence into Europe (Otranto et al., 2011). Adult worms are found under the conjunctival membranes, and are commonly known as eyeworms. Muscid flies act as vectors, taking up the first-stage larvae (L1), and depositing the L3 during feeding on lachrymal secretions. Irritation by the presence of the adult worms causes pain, blepharospasm, sometimes ulceration, and profuse lachrymation, which attracts fly vectors. Human infection is rare but has been reported, and manifests as pain and conjunctivitis, and the sensation of a foreign body in the eye. Infections may be self-limiting, but physical removal of the worms is recommended.

## Strongyloidosis

*Strongyloides stercoralis* is known as the intestinal threadworm, and parasitizes the small intestine of dogs as well as humans and other primates. It has a tropical distribution. Infection causes mucosal disruption and a protein-losing enteropathy, which manifests as diarrhoea and emaciation. Infections are most usually selflimiting, but in immuno-suppressed patients (canine and human), infection can generalize to other organs, with fatal consequences (Stewart et al., 2011). The parasite can persist asymptomatically for many years, causing disease following subsequent immuno-suppression. Only females are parasitic, producing eggs by parthenogenesis that pass out in the faeces, hatch to L1, and develop to the L3 stage. L3 can infect a new host, continuing the cycle, or develop into free-living male and female adult worms, which maintain a population outside the host (Viney, 2006). Infection is by penetration of the skin, followed by migration to the intestine. Although S. stercoralis infects both dogs and humans, human-to-human transmission occurs, so the zoonotic importance of canine infection is probably limited to relatively few cases.

## Other Nematodes

A number of other nematodes infect both dogs and humans, but cases of zoonotic transmission are either rare, or likely to come from animal hosts other than from dogs. These include the nasal and respiratory worms in the genera *Capillaria* and *Eucoleus*, the kidney worm *Dioctophyma renale*, and the Guinea worm *Dracunculus melitensis*. Given the minor role of dogs in the epidemiology of human disease, these are not considered further.

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# **10** Dogs and Ectoparasitic Zoonoses

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Increasingly, human beings and their pets are sharing the same environment, and because canine ectoparasites have varying host specificity, man is at risk of acquiring some of these infestations. However, the practice of 'one medicine' is still relatively rare, as evidenced by many publications in the literature attesting to a lack of co-operation between medical and veterinary specialists which has limited the precision with which diagnoses are made. Indeed, one has to go back to the 1970s to find a publication detailing a large case series of canine ectoparasitic zoonoses that resulted from collaboration between medical and veterinary dermatologists (Hewitt *et al.*, 1971). This publication is arguably the most comprehensive description of the disease problems. Most commonly reported were fleas, affecting 100 individuals, followed by scabies, which affected 65; Cheyletiella, which affected 45 patients; and three who were possibly suffering from Otodectes infestation. This chapter will discuss these four parasites.

## Insecta

## Fleas

### Biology

Fleas are brown, wingless insects approximately 3–4 mm in length. They belong to the on dogs and cats worldwide, and has limited host specificity. It has been the predominant species found on dogs in studies conducted in many parts of the world over the last 25 years (e.g. Harman et al., 1987; Alcaino et al., 2002; Durden et al., 2005; Beck et al., 2006; Bond et al., 2007; Gracia et al., 2008). Ct. canis was very much the minor species in all regions and was not found in one survey (Harman et al., 1987). Other species found in small numbers were Archeopsylla erinacei, Pulex irritans, P. simulans, Echidnophagia gallinacea (the 'stick-tight' flea), and a number of minor species whose natural hosts are rodents and other wildlife. In some colder climates such as northern Scandinavia. Ct. felis does not survive, and flea infestation is acquired from wildlife. However this is generally short-term with spontaneous resolution. The major problem is thus *Ct. felis*, and this will be the focus of this discussion. Of concern also are the other hosts of Ct. felis that may aid in the spread of infestations, and that may have to be considered in any control strategy. It is found on foxes, raccoons, opossums, and ferrets, but rarely if ever on squirrels, rabbits,

order Siphonaptera, which comprises in excess

of 2000 species and sub-species. Ctenocephalides

felis is the subspecies most commonly found

Mating occurs after a blood meal, and the pearly white eggs are laid on the host, but usually fall to the ground where the three

and birds (Dryden and Rust, 1994).

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larval stages are completed. Larvae are positively geotactic and negatively phototactic, burrowing deep into carpets and cracks and crevices in the flooring (Dryden and Rust, 1994). The third-stage larvae are around 4–5mm in length, and produce a silk-like cocoon in which pupation occurs. This is the most resistant phase, and can last for some months. The entire life cycle can be completed in as little as 14 days, but it commonly takes 3–4 weeks.

The environmental conditions favourable to the development of the different life stages of Ct. felis have been investigated in detail (Silverman and Rust, 1981). A relative humidity of 70-80% and a temperature of 30°C are optimal for most stages of the life cycle. They do not do well at very high humidity and high temperatures, or at low humidity and high temperatures. Thus in North America they are absent from the desert south-west and from high altitudes. They are also absent from the more northern parts of Canada. In Europe they are absent from northern parts of Scandinavia. However in some areas of Sweden from which *Ct. felis* was previously absent, it is now encountered not uncommonly. Whether this has resulted from better adaptation to adverse conditions, or from global warming, is unclear.

#### Flea infestation in the dog

The adult is stimulated to emerge by vibrations, heat, and  $CO_2$ . There is often a massive, simultaneous hatch when premises have been left empty for some time, and sometimes a bimodal hatch occurs. Host-seeking is likewise aided by light, movement, and  $CO_2$  (Dryden and Rust, 1994). Once on the dog, fleas tend to have a predilection for the stomach and hindquarters. Fleas can lead to a severe dermatitis when the pet is hypersensitive, but they can also have other effects on the host.

It is likely that all dogs that develop dermatitis due to fleas are in fact allergic to the salivary antigens (Fig. 10.1). Flea saliva contains multiple protein allergens that are recognized in varying combinations. The major allergen, Cte f 1, has been cloned and is recognized by sera from some 90% of hypersensitive dogs (McDermott *et al.*, 2000). Flea allergy dermatitis



**Fig. 10.1.** The flea bites to suck blood, and in so doing injects salivary antigens.

has a complex immunopathogenesis, involving both immediate (IgE) and delayed (cell-mediated) hypersensitivity (Gross and Halliwell, 1985) and also cutaneous basophil hypersensitivity (Halliwell and Schemmer, 1987). Other studies have shown that (i) all dogs can become allergic to fleas if intermittently exposed, and that continual exposure is protective (Halliwell, 1990); (ii) atopic dogs are predisposed to the development of flea allergy, and that the degree of hypersensitivity wanes in the older dog (Halliwell et al., 1987); and (iii) dogs who are continually exposed to fleas and do not develop dermatitis are, at least in part, immunologically tolerant (Halliwell and Longino, 1985).

The primary eruption in flea allergy dermatitis is a papule (Fig. 10.2), which may crust over. Occasionally frank urticaria may be seen. Self-trauma leads to a range of secondary changes including widespread erythema and hair loss with a distribution that follows that of the fleas on the host (Fig. 10.3). The diagnosis of flea allergy dermatitis is established by observing compatible clinical signs, the presence of fleas or flea faeces, and the demonstration of hypersensitivity. The latter is best achieved by intradermal tests using a reliable flea antigen, and observing for immediate (15 min) and/or delayed (48 h) reactions. Serology for flea antigen-specific IgE will not identify those animals suffering from delayed hypersensitivity alone (some 15%).

When both dog and owner in the same household are pruritic, attention is readily drawn to the possible source of the human



Fig. 10.2. Papular eruptions resulting from flea bites in a dog.



**Fig. 10.3.** Extensive hair loss and inflammation resulting from flea-bite hypersensitivity in a dog.

skin disease. More troublesome in terms of making the correct association are dogs harbouring fleas and showing no clinical signs. A careful assessment is needed to establish the presence of fleas in such cases. Use of a flea comb many be helpful, and some recommend vigorous brushing of the coat and collection of the resultant debris for subsequent examination. Faeces are identified by placing the debris on a moistened white paper, to which they will impart a reddish-brown colour.

The non-allergic effects of fleas on dogs include anaemia, transmission of the dog tapeworm *D. caninum*, and the non-pathogenic filarid *Dipetolonema reconditum*.

#### Zoonotic implications

Fleas can infest man when they hatch in a contaminated environment or by movement

from the canine host. The fleas are especially aggressive when the house has been empty for a period, and in such cases they usually attack the ankles and lower limbs. White socks are known to attract the fleas, and indeed have been used to estimate flea numbers in an environment. Second, they may transfer to family members when they lie close to the animal, or stroke it. In this case, the distribution is more generalized. The classical primary lesion is papular urticaria. Lesions consist of grouped papules that commence with irregular urticarial wheals some 5-10mm in diameter (Hewitt et al., 1971). After 24h these are replaced by small pruritic papules. In severe cases, a widespread papular rash develops leading to self-excoriation and lichenification. Ulceration and lichenified plaques may ensue in chronic cases, and become secondarily infected. The clinical signs may be severe enough to prompt relocation of the family to a flea-free area.

It is likely that the progression of the eruption reflects different aspects of the immunopathogenesis. It is assumed that both immediate and delayed hypersensitivity occur in man, although this does not appear to have been investigated as thoroughly as in the dog. However, one recent study of patients suffering from papular urticaria has demonstrated a Th1/Th2 imbalance (Cuéllar *et al.*, 2009).

Of perhaps greater zoonotic significance are diseases that Ct. felis can transmit. The dog tapeworm D. caninum can, on occasions, affect man and especially children (Jones, 1979). Murine typhus is ordinarily a mild febrile illness causing headaches, chills, skin rashes, and occasionally a more serious disease involving the kidneys and CNS. The disease occurs in man and many small mammals, and the causative organism, *Rickettsia typhi*, can be transmitted by *Ct. felis*, although the major vector is the oriental rat flea, Xenopsylla cheopsis (Farhang-Azad et al., 1984). Ct. felis has also been shown to be able to transmit Yersinia pestis, the causative organism of bubonic plague. The emergence of feline plague as a significant problem in the western United States, not only in domestic cats but also in wild felids (Bevins et al., 2009), has emphasized the important role

that cats and Ct. felis can play in transmission to man. Experimental infection of cats gives rise to a disease very similar to that in man (Watson et al., 2001), and a report details 23 cases of human plague, five of which were fatal, attributed to feline contact (Gage et al., 2000). Of course, this concerns cats, and not dogs, but the ease with which Ct. felis can move between these two species implies that infection from Ct. felis carried by dogs is not impossible. Finally, mention must be made of cat scratch disease and the causative organism Bartonella henselae. This organism ordinarily causes subclinical disease in cats, but some animals may show a transient anaemia, fever, and occasionally neurological signs (Kordick et al., 1999). In chronic cases lymphadenopathy, gingivitis, stomatitis and fever may occur (Breitschwerdt and Kordick, 2000). Transmission to man is believed to occur through flea faeces, which are inoculated by the scratching or biting of the cat (Foil et al., 1998). Although fever and lymphadenopathy are the signs classically associated with cat scratch disease in man, a range of far more serious clinical signs may be seen, especially in immunosuppressed patients (Breitschwerdt, 2008). More recently, epidemiological studies of antibody prevalence in different populations have fuelled speculation that the dog may also be a reservoir for Bartonella henselae (Henn et al., 2005, Solano-Gallego et al., 2004). A variety of chronic diseases in turn have been attributed to the infection in dogs, including granulomatous hepatitis, peliosis, and epistaxis (Chomel et al., 2006). Thus there exists a clear possibility that dogs, through their carriage of Ct. felis, could be a source of this important disease of man.

#### The treatment of canine flea infestation

Twenty years ago, flea control largely comprised the use of pyrethrins, pyrethroids (their synthetic analogues), and organophosphates – the latter being used at some risk to both owner and pet. However, the past two decades have seen the development of some remarkable new chemicals, some of which are now available as 'over-the-counter' products. It is none the less essential that professional advice be obtained, and a safe and effective strategy developed, taking into account (i) the extent of the infection, (ii) the presence and habits of other animals in the house, (iii) the lifestyle, and (iv) the inside and outside environment and the likelihood of reinfestation. A brief description of the newer adulticides follows:

- Fipronil (Frontline<sup>®</sup>, Merial). Available as a spray or spot preparation for dogs and cats.
- Imidocloprid (Advantage<sup>®</sup>, Bayer). For spot-application to dogs and cats.
- Selamectin (Stronghold<sup>®</sup> or Revolution<sup>®</sup>, Pfizer). For spot-application to dogs and cats.
- Nitenpyram (Capstar<sup>®</sup>, Novartis). Shortacting (24h), administered orally for dogs and cats.
- Metaflumizone (ProMeris<sup>®</sup>, Fort Dodge). For spot-application to dogs and cats. Also available with amitraz as ProMeris Duo<sup>®</sup> for dogs only.
- Pyriprole (Prac-tic<sup>®</sup>, Novartis). For spot application to dogs only.
- Spinosad (Comfortis<sup>®</sup>, Eli Lilly). For oral administration to dogs only.
- Dinotefuran (Vectra<sup>®</sup>, Ceva). Topically to dogs with permethrin and pyriproxifen (Vectra 3D) and with pyroproxifen alone for cats.
- Indoxacarb (Activyl<sup>®</sup>, MSD). Monthly spot-on formulation for dogs and cats.

Not all of these products are available in all countries of the world.

All animals in the home must be treated with an effective adulticide; in addition, thought must be given to interrupting the life cycle. This can be accomplished by the use of insect development inhibitors (IDIs) or insect growth regulators (IGRs). An example of an IDI is the chitin synthesis inhibitor, lufenuron (Program<sup>®</sup>, Bayer) which is administered orally once per month to dogs, and is available as a 6-monthly injectable for cats. The IGRs include the triazine derivative, cyromazine, and the juvenile hormone analogues (JHAs) fenoxycarb, methoprene, and pyriproxifen. Cyromazine is administered orally, and interferes with chitin deposition rather than with its synthesis. The mode of action of the JHAs is quite different. Normal pupation is initiated by a fall in the level of insect juvenile hormone,

and if JHAs are present in the environment, pupation is prevented. They are also ovicidal and larvicidal (Dryden and Rust, 1994). The JHAs are available for on-animal use, as well as for environmental application – often in combination with an adulticide such as the pyrethroid, permethrin. Of the three that are the most widely used, methoprene is sensitive to ultraviolet light, and thus has a limited duration of action; pyriproxifen and fenoxycarb are stable, and persist for many months in the environment. Indeed pyriproxifen is so effective that concerns have been expressed over the possible effects on friendly insects when used outdoors.

A number of flea repellents are marketed, but none have been shown to be efficacious in independent, controlled trials.

In tropical and subtropical climates, the external environment can be an additional source of reinfestation – particularly if there are free-roaming cats. Organophosphates are commonly used for control, concentrating on shady areas where there is plenty of organic debris. Larvae cannot survive in open areas exposed to direct sunlight.

Complete and effective flea control is now entirely possible with an appropriately formulated programme, but careful attention must be paid to its development, and the agreed plan must be rigorously adhered to.

## Arachnida

#### Mites: Sarcoptes scabiei var. canis

## Biology

Adults are white, oval-shaped globose mites measuring 200–400  $\mu$ m in length (Fig. 10.4). There are two pairs of anterior legs bearing long stalks with suckers, and two pairs of posterior legs bearing bristles alone. Copulation takes place on the skin surface in moulting pockets, with the female then burrowing into the epidermis where she lays eggs. After hatching, the 6-legged larvae moult into 8-legged nymphs, and then into adults at which point they merge onto the surface. The entire life cycle can be completed in as little as 3 weeks.



**Fig. 10.4.** *Sarcoptes scabei* adult mite and eggs. Faecal pellets are also visible.

#### The infection in dogs

In the majority of cases the disease is acquired from infected dogs. However, dislodged mites can remain viable for up to 19 days under optimal conditions of 10°C and 97% relative humidity (Arlian et al., 1984a), and so acquisition of infection from the environment is quite possible. Consequently, pet shops, dog shows, and veterinarians' offices represent possible sources of infection. Direct or indirect contact with wildlife represents other likely sources of infection. Dependent upon the geographic location, infection can be acquired from foxes (Davidson et al., 2008), badgers (Collins et al., 2010), ferrets (Phillips et al., 1987), racoons (Ninomiya and Ogata, 2005), and rabbits (Arlian et al., 1984b). A report from Sweden identified Sarcoptes scabiei var. canis in wild lynx, pine martin, wolf, and mountain hares (Mörner, 1992). Cats represent another possible source. Although infectivity for this species appears to be quite low, sporadic cases are reported, with a recent report documenting four cases (Malik et al., 2006). In two instances the infection was apparently acquired from foxes, whilst the other two cases had close contact with infected dogs. Interestingly, the clinical signs were more suggestive of Norwegian (crusted) scabies with little pruritus, than of feline scabies that is ordinarily caused by Notoedres cati.

Penetration is achieved within 30min and is aided by a mite secretion that dissolves host tissue. As might be expected, the intradermal deposition of antigen normally provokes a strong immune response which leads to marked inflammation, and affects the disease outcome. It has been shown that when normal dogs are infected experimentally, a proportion will in time self-cure (Bornstein, 1991). This self-cure is enhanced when animals are rechallenged after treatment with an ectoparasiticide. Immunohistochemistry has shown that self-cure is accompanied by an influx of CD4+ T cells, both T-helper and inducer cells, together with neutrophils (Arlian et al., 1997). Similar findings have resulted from a study of the epidemiology in Norwegian red foxes, suggesting that subclinical infection and self-cure can lower the incidence of overt disease in the population (Davidson et al., 2008). Taken together, the above data suggest that a strong Th1 response is associated with protection, whereas a Th2 response is associated with susceptibility. In support of this, it is frequently noted that mites are more readily demonstrable in corticosteroid-treated dogs than in animals not so treated. It is a matter of conjecture as to which arm of the immune response is responsible for the profound pruritus that is a feature of the disease. In part, of course, this could result from triggering of the itch receptors at the dermoepidermal junction by the mechanical effects of the mites burrowing within the epidermis.

One fascinating clinical variant of scabies, both in man and the dog (Patterson, 1995), is Norwegian or crusted scabies. This is accompanied by severe crusting and a near absence of pruritus. Mites are demonstrable in large numbers, implying a failure of the protective immune response. In man this is regularly associated with immunodeficiency diseases such as HIV/AIDS (Corbett et al., 1996). Recent studies of Norwegian scabies in man have shown a predominance of CD8+ T cells infiltrating in the dermis, with relatively few CD4+ cells, and high levels of IgE and IgG (Walton et al., 2008). No such studies have been undertaken in dogs, but the striking similarities of the disease in man and dog suggests that the same underlying immunopathogenesis is likely.

Scabies affects predominantly younger dogs, which suggests an age-related immunity, and there is no sex or breed predisposition (Feather *et al.*, 2010). The disease usually commences in the less-haired areas, such as the ear margins, elbows, and ventral chest – probably reflecting the greater ease with which transmission occurs in those areas. The primary eruption is a papule and burrows may be visualized (Fig. 10.5). A variety of changes may result from self-trauma, leading to extensive areas of hair loss, hyperkeratosis, and crusting. The disease may spread to involve large areas, which are usually symmetrical, but the dorsum is ordinarily spared. Occasional cases are reported with a localized distribution (Pin et al., 2006). The extreme pruritus that accompanies the disease often leads to cachexia, as sleep is prevented and inappetance may develop. Proteinuria may be seen, which is likely to result from an immune-complex glomerulonephritis (Baker and Stannard, 1974).

A diagnosis of scabies in dogs is not easy to confirm due to the paucity of mites in the lesions. The clinician will first look for clinical and historical signs that raise the index of suspicion. Has there been an opportunity for contagion? If the disease is very pruritic, and (if so treated) is it only partially corticosteroidresponsive? Are other dogs affected, and are the owners affected? Are the clinical signs suggestive? Another useful indicator is the pinnal-pedal reflex. The edge of the pinna is rubbed between the thumb and forefinger, and a positive response is shown by involuntary attempts to scratch with the hind limbs. In a recent study, a positive response resulted in 82% of 55 dogs with confirmed scabies (and 90% of those with overt pinnal disease), as compared with 6.2% of 533 dogs with other miscellaneous pruritic dermatoses.



**Fig. 10.5.** Severe, erythematous papular eruption in a dog due to scabies.

This translates to a specificity of 93.8% and a sensitivity of 81.8% (Mueller *et al.*, 2001).

A definitive diagnosis is made by demonstration of mites via skin scrapings in mineral oil. The hair is gently trimmed away from an involved area, and the skin moistened with oil. Remembering that the males live on the surface and the females within the epidermis, it may be helpful to take a very superficial scraping, and then return to the same area for a deeper scraping. Nonetheless, however carefully the scrapings are performed, they may be positive in as few as 20–40% of cases.

If skin scrapings are negative, and the index of suspicion is still high, serology may be undertaken. This is widely available in Europe, although not as yet in North America. One study showed an 84.2% sensitivity and 89.5% specificity (Lower et al., 2001), with another showing both a sensitivity and specificity of 100% when borderlines were eliminated (Curtis, 2001). There is some evidence of cross-reactivity between mite species, and so an important finding in the latter study was that, of 12 atopic dogs that were positive to Dermatophagoides farina, all were negative on sarcoptes serology. Positive serology may result for up to 4.5 months after successful treatment (Lower et al., 2001).

Ultimately, if there is still a suspicion of scabies even in the light of negative results to all appropriate tests, a therapeutic trial with an appropriate parasiticide should be undertaken.

### Zoonotic implications

The acquisition of infection reportedly occurs between 1 and 10 days after exposure (Charlesworth and Johnson, 1974), but recent observations in a veterinary school suggests that clinical signs may occur within 6h of contact with an affected animal (T. Paterson, pers. comm., Grenada, 2011). Infection after even prolonged contact is not inevitable, and in one report of an 'epidemic', some children who had close contact were not infected (Charlesworth and Johnson, 1974). The factors that determine the likelihood of infection are not known, but it has been hypothesized that prior contact with the mite and consequent sensitization may facilitate the establishment of an infection. Although close contact with the affected dog is usually reported, cases are encountered wherein no direct contact has occurred, and indirect infection from the environment is assumed (Charlesworth and Johnson, 1974). The sites involved reflect those most likely to be in the closest contact with the infected animal, which are frequently the forearms, abdomen, waist, and trunk. Lesions may localize in the region of the belt or bra straps. The initial eruption is a papule, and concomitant vesicles may develop. In some cases urticarial lesions are observed. The lesions are intensely pruritic, and the pruritus is often worst at night and after bathing (Emde, 1961; Beck, 1965). In contrast to human scabies, burrows are not seen.

There is an interesting report (Ruiz-Maldonado et al., 1977) of a case of Norwegian scabies in a child suffering from Turner's syndrome - a genetic condition characterized by multiple endocrinopathies and also immune dysfunction (Rongen-Westerlaken et al., 1991). As noted earlier, the propensity to develop this condition rather than classical scabies may reflect a Th1/Th2 cell imbalance (Walton, 2010). Pruritus in this patient was inconstant and mild, and lesions were characterized by extensive crusting. When the patient slept with other family members, they developed severe pruritus with characteristic papular eruptions. Mites were abundant among the crusts, and skin scrapings yielded a mean of 56 mites per 10g of crust. Three dogs in the family were diagnosed with scabies, and a normal dog was infected by application of crust material from the child, with typical canine scabies resulting.

The course of canine scabies infection in man is usually short, resolving within a few days of removing or treating the infected dog. Parasiticidal therapy is not generally required, as the current view is that the mite cannot complete its life cycle on man. However, the time taken for resolution is very variable, and may be up to 3 weeks (T. Paterson, pers. comm., Grenada, 2011), which might suggest multiplication of the mites. In a study attempting to address this, two human volunteers were infected with canine scabies mites under tightly controlled conditions (Estes *et al.*, 1983). Each received 14 adult female mites taken from a case of canine scabies. After 96 h, eight live mites were recovered from each volunteer. Shave biopsies revealed that eight and nine eggs, respectively, had been deposited in burrows on each recipient, and one egg from each was observed to hatch. At this point the experiment was terminated. The conclusions were that there is at least the potential for completion of the life cycle in man. For these reasons, it would seem prudent to prescribe parasiticidal therapy, if the clinical signs persist for more than a few days after removal or control of the source of infection.

#### Treatment of canine scabies

The availability and licensing of scabicidal drugs varies widely in different countries of the world. In the United States, a 2.5% lime sulphur dip is available and effective. It has a wide safety margin, but an unpleasant odour and may stain light-coloured coats. Amitraz dips, using the protocol licensed for demodecosis, are effective (Folz et al., 1984), but anecdotal evidence suggests that resistance may be acquired during treatment. A metaflumizone and amitraz combination has been shown to give a cure rate of 83% when applied biweekly (Fourie et al., 2007), but the propensity for this drug to cause pemphigus foliaceus-like drug eruptions limits its usefulness (Oberkirchner et al., 2011). Fipronil spray appears to be both safe and effective (Curtis, 1996; Terada et al., 2010).

Newer approaches to the therapy of canine scabies have focused mostly on the macrocyclic lactones, and in particular on the avermectins (ivermectin and selamectin) and the milbemycins (milbemycin and moxidectin). Ivermectin is widely used at 200–400 µg by subcutaneous injection biweekly, or orally at the same dose, or at a higher dose of 500 µg topically (Paradis et al., 1997). Indeed, many practitioners use this as a diagnostic aid, but this may be inappropriate following the first report of ivermectin-resistant scabies in dogs (Terada et al., 2010). Of importance is the fact that this drug is not licensed for use in dogs for this purpose in any country of the world. It is highly toxic in herding dogs which have the MDR1 mutation, and toxic reactions are also sometimes encountered in dogs believed to be lacking this mutation. Less toxic, and more appropriate for routine use are milbertycin at 2.0 mg/kg weekly (Miller et al., 1996), and an imidocloprid/moxidectin combination (Advocate<sup>®</sup>, Advantage Multi<sup>®</sup>, Bayer Animal Health) (Fourie et al., 2006). Recent studies on demodecosis have shown that this product is more effective and perfectly safe when administered weekly instead of monthly (Paterson et al., 2010). The broad-spectrum avermectin, selamectin (Revolution®, Stronghold®, Pfizer), is licensed for the treatment of scabies worldwide, and is highly effective. However, it is somewhat slow to act; live mites were still found 30 days after the first application, albeit in very low numbers (Shanks et al., 2000).

In view of the fact that live mites can persist in the environment for significant periods, the use of a premise spray such as permethrin would appear to be desirable practice.

#### Cheyletiella spp.

#### Biology

*Cheyletiella* spp. are large mites, some 400– 500  $\mu$ m in length, that are just visible to the naked eye. They have four pairs of legs ending in combs, and their most characteristic feature is the presence of accessory mouthparts that end in a pair of sharp hooks (Fig. 10.6). The species most commonly found on dogs is *C. yasguri* (Smiley, 1965), while



**Fig. 10.6.** *Cheyletiella* mite seen in a skin scraping from an infested dog.
rabbits typically harbour C. parasitivorax, with C. blakei infesting cats (McKeever and Allen, 1979). However Cheyletiella are not highly host-specific, and the species found on domestic pets will depend upon the source of infection. Thus when the infection is acquired from rabbits, dogs will frequently harbour C. parasitivorax. The mites are obligate parasites, and ordinarily die within 48 h of removal from the host. However, if kept refrigerated they may live for up to 10 days (Foxx and Ewing, 1969). The life cycle is completed on one host, proceeding from eggs through larval and nymphal stages to the adult, in approximately 3-4 weeks. The mites do not burrow, but when not moving around on the skin, are contained within pseudotunnels of epidermal debris. Often they will cause the scale to move causing the 'walking dandruff' that is characteristic of the infestation. They periodically attach themselves firmly to the epidermis, and then pierce the skin with their stylet chelicerae and feed on tissue fluids. The eggs may fall off into the environment, but if not, they are attached to hair shafts by a cocoon-like structure of closely woven fine threads (Foxx and Ewing, 1969).

#### Cheyletiella infestation in dogs

The infection is acquired from either direct or indirect contact with infected dogs, cats, or rabbits. Pet shops, grooming parlours, dog shows, and veterinarians' offices are all possible avenues of infection. Although live adults have a limited lifespan off the host, the hatching of eggs that have fallen from the host can be a ready and constant source both of infection and of re-infection. Other dogs and/or cats in the household, of course, are a very important source. However it is not inevitable that all dogs and cats that live in close proximity will become infested. Also, some may become infested but remain asymptomatic as carriers. This is an important consideration when considering control.

There has been little work done on the immune response to *Cheyletiella*, but the very varied host response suggests that an allergic response and possibly also protective immunity may occur. For example, it is said – although with little documentation

- that the disease is both more common and more severe in puppies (Cohen, 1980). One study looked for evidence of any correlation between the level of infestation as judged by mite recovery, and the clinical severity. None was evident (Saevik et al., 2004). Although no antigen is currently available, Dermatopagoides farinae and D. pteronyssinus extracts have been employed for intradermal testing in affected animals, relying on putative cross-reactivity (White et al., 2001). Thirteen of 23 affected animals gave positive reactions to D. farinae, and 12 to *D. pterynossinus*. One month later, after successful treatment, of those dogs which had previously shown positive IDT reactivity, four and seven of them, respectively, gave negative intradermal tests to the two antigens.

The clinical signs are quite variable, but generally consist of scaling with pruritus, both of which can range from minimal, or even absent, to severe. The scaling is predominantly dorsal, or dorsolumbar, but may extend to the flanks or become generalized. In some 15% of cases, an oily haircoat, rather than scaling, may be the presenting sign (White et al., 2001). The localization of pruritus does not always coincide with the area of the most severe scaling, and is generalized in the majority of cases (Saevik et al., 2004). In heavy infestations, the mites can be visualized – especially when examined with a magnifying lens – and the scale may move from the activity of the mites. In chronic cases, areas of crusting which represent pseudotunnels may be palpable (Ayalew and Vaillancourt, 1976).

As with scabies, the first consideration in establishing the diagnosis is to assess the index of suspicion before pursuing confirmation by the identification of mites or eggs. A carefully taken history must assess whether there been an opportunity for contagion, such as meeting other dogs or cats, or being in an area frequented by rabbits. The possibility of infection from a contaminated environment should also be assessed. All in-contact dogs and cats should be examined for clinical signs of infection, and enquiry should be made of all humans who have contact with the pets, to assess whether any are suffering from dermatological signs compatible with chevletiellosis.

A recent study examined the efficacy of a number of different approaches to obtaining diagnostic samples from the skin of affected animals (Saevik et al., 2004). Vacuuming with a specially adapted capture system was the most efficient. Impressions employing clear cellulose tape pressed firmly on the skin yielded positive results in 73.1% of 26 cases, and skin scrapings were positive in 40.9% of cases. Using the latter techniques, the hair should be carefully trimmed from the site to be sampled, and skin scrapings should be very superficial, and taken from areas premoistened with mineral oil. Hair pluckings to examine for evidence of eggs attached to the hair shaft were positive in 54.2% of cases. Eggs may also be found in routine examination of faeces (McGarry, 1993), but there are no data on the sensitivity of this approach in achieving a diagnosis.

#### Zoonotic implications

It is certain that *Cheyletiella* affects man with a far greater frequency than is diagnosed. The ease with which infection is acquired will, of course, depend on the closeness of contact between man and dog. Some years ago, Walton (1974) diagnosed 102 dogs with *Cheyletiella*, and 83 of the individuals in direct contact with the dogs reported a pruritic dermatitis consistent with *Cheyletiella* infection, which suggests that the infection is readily transmitted.

The primary lesion in man is generally an erythematosus papule which may be surrounded by a fragile vesicle (Cohen, 1980). The papules are usually found in small groups, but may be widely scattered. They do not become confluent. Chronic lesions frequently become pustular, and may develop a yellow necrotic centre (Rivers et al., 1986) - which some view as pathognomonic for Cheyletiella (Hewitt et al., 1971). Lesions ordinarily resolve within 3 weeks, as long as the source of infection is controlled. Less frequently there may be papular urticaria, with a halo of erythema (Shelley et al., 1984), or more extensive urticarial lesions. Rarely, bullous lesions may develop (Dobrosavljevic et al., 2007), and lesions mimicking erythema multiforme and dermatitis herpetiformis have been reported

(Hewitt *et al.*, 1971), as has generalized pruritus without evidence of lesions. Burrows are not seen, and mites are not recovered from affected patients, indicating that contact is generally brief. The distribution typically involves the lower chest, abdomen, forearms, and the anterior thighs, but may extend to the face and scalp. One patient was reported to become systemically ill, with elevated immune complexes, numbness of the fingers, and arthalgia (Dobrosavljevic *et al.*, 2007). The signs resolved spontaneously following successful treatment of the infected animal.

Biopsies reveal a typical picture of an insect bite reaction, characterized by a perivascular lymphocytic infiltrate accompanied by eosinophils (Maurice *et al.*, 1987). Little is known of the immunological response of patients, but in one case a delayed hypersensitivity was evident upon intradermal testing (Maurice *et al.*, 1987).

Parasiticidal therapy of affected humans is unnecessary, and resolution invariably follows successful treatment of the implicated animal(s).

#### Treatment of canine Cheyletiella infection

As Cheyletiella is a surface-dwelling mite, it is more readily susceptible to parasiticidal agents than is Sarcoptes scabei. Most of the commonly used insecticides are effective, including pyrethrins and pyrethroids, but with the exception of imidocloprid. Although no products have a specific claim for *Cheyletiella*, there are published data documenting the efficacy of selamectin (Fisher and Shanks, 2008), fipronil (Chadwick, 1997; Scarampella et al., 2005), milbemycin (White et al., 2001), ivermectin (Pagé, et al., 2000), and permethrin (Endris et al., 2000). Lime sulphur, amitraz, and selenium sulphide are also reportedly effective. The human literature contains many reports of reinfestation resulting from inadequate control, and care must be taken to treat all dogs, cats, and rabbits with a product appropriate for that species, irrespective of whether the animals appear to be infected. Attention must also be paid to the environment. All bedding, grooming equipment, etc., should be washed at a high temperature, and then treated with a parasiticide. Carpets and any furniture

frequented by the pets should likewise be treated with a parasiticide. Proprietary products marketed for environmental flea control containing a pyrethroid and insect growth regulator are appropriate for this use. Despite the fact that there is no documented evidence on the effect of juvenile hormone analogues on the eggs and larval stages, they are very likely to be efficacious.

#### Otodectes cynotis

#### Biology

Otodectes cynotis is a non-burrowing psoroptid mite, and an obligate parasite. It parasitizes the ears of dogs and cats, and may also affect wildlife including arctic foxes (Gunnarsson et al., 1991) and the Eurasian lynx (Degiorgis et al., 2001). It is just visible to the naked eye, measuring up to  $500\,\mu\text{m}$  in length. The mites have a greyish appearance, and otoscopic examination of the ear canal shows them to have the appearance of cigarette ash. The life cycle is completed in around 3 weeks, with the mites feeding on epidermal debris. They can persist in the environment for up to 17 days at 95% relative humidity and 10°C (Milillo et al., 2004). Although primarily an otic parasite, they may leave the ear canal and be found elsewhere on the body.

#### Otodectes infection in dogs

There are no recent data on the proportion of cases of canine otitis externa in which Otodectes infection is implicated, but it is estimated to be around 10%, which is a lower proportion than seen in cats. Young animals appear to be particularly susceptible. The degree of pruritus is extremely variable, with some animals being asymptomatic, whereas others may develop extreme pruritus. The level of pruritus does not appear to be related to the mite burden, and is likely to be dependent on the extent to which secondary bacterial and/or yeast infection develops, and also on the presence of hypersensitivity. Immediate hypersensitivity has been demonstrated in the cat (Powell et al., 1980), and indeed this was the first demonstration of the existence

of reaginic antibody in this species. However, no such studies have been undertaken in the dog. As noted above, the mites may sometimes leave the ear canal, and can be widely distributed on the body, and rarely may be the cause of generalized pruritic dermatitis (Kraft *et al.*, 1988).

Diagnosis is made by observation of the mites and/or eggs in exudate from the ear canal, carefully removed by a cotton-tipped applicator moistened with mineral oil, or by skin scrapings if there is extra-otic involvement.

#### Zoonotic implications

Man is rarely affected by Otodectes. In an early detailed study in the United Kingdom involving both veterinary and medical investigations, mites were found in dogs or cats in 3 of 173 cases in which zoonotic insect bites were suspected (Hewitt et al., 1971). Lesions similar to those produced by Sarcoptes were seen, but it is always difficult to prove a cause-and-effect relationship. For example, in one case in Denmark, both *Cheyletiella* and Otodectes were found on the incriminated pet (Kristensen, 1978). This prompted the writer to speculate that a previous report of a case of presumed Otodectes dermatitis from California might in fact have been due to Cheyletiella (Herwick, 1978). However, there is a convincing report of otitis with tinnitus in a patient, which resolved following appropriate acaricidal therapy (Van den Heyning and Thienpont, 1977). Even more convincing was a report by Lopez (1993), a veterinarian, who infected his ear canals with Otodectes mites. He observed that the mites tended to vacate the ear canal during the night and walk over the face. The pruritus was quite intense, as was the degree of tinnitus. Both diminished with time, and were much less on reinfestation, which suggested a protective immune response.

#### Treatment of Otodectes in dogs

The ears should be flushed with saline to remove as many of the mites and eggs as possible, followed by application of an ectoparasiticide-containing proprietary otic product. If it is suspected that the infestation has spread from the ear canal, then the entire body should be treated; indeed, many clinicians prefer to use this approach in every case. All of the common parasiticidal agents are effective, with the exception of imidocloprid. There have been published reports confirming the efficacy of a moxidectin/imidocloprid combination (Kreiger *et al.*, 2005) and also of selemectin (Blot *et al.*, 2003). This should be supplemented by appropriate environmental control, for example the use of a permethrin/ pyriproxifen combination.

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# **11** Dog Population Management

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Archaeological evidence for a close association between humans and dogs dates back to around 12,000–14,000 years ago (Morey, 2006); however, genetic evidence suggests that the separation of the domestic dog from a common ancestor with the wolf may have occurred far earlier, some indicating a date greater than 100,000 years ago (Vila *et al.*, 1997). This first separation of species may well have been due to the predecessor of the domestic dog associating itself with early human hunters in order to benefit from scavenging, hence a drive by dogs to coexist with humans as opposed to a human attempt at domestication.

Since humans became involved in dog domestication, and later in very focused artificial selection for breeds with specific physical and behavioural traits, the roles that dogs have fulfilled in human society have been many and varied. Some of these have stood the test of time, such as the role as a 'watch dog'. Even the earliest domestic dogs benefited human settlements by warning them of approaching predators or strangers, using their acute senses of smell and hearing, and the same capacity is still valued by dog owners today. In recent years there has been a proliferation of the roles 'assistance dogs' can fulfil for people; from the original guide dogs for the blind which were first formally trained in Germany following

World War I to dogs that can indicate to an epilepsy sufferer the early stages of an oncoming seizure. Dogs' superior sense of smell has also been exploited by people to help locate substances such as drugs, explosives, ivory, or humans. Dogs have even been shown in proof-of-principle studies to be able to detect tumour-related volatile compounds in urine samples of people diagnosed with bladder cancer (Willis *et al.*, 2004). But by far the most common role for dogs, and one that is found in all countries of the world, is as a companion for humans.

Both the roles that dogs fulfil and local cultural norms will impact on how dogs are kept by people; in some countries they are confined on private property and are accompanied by an owner whenever they leave that property; in other countries dogs are allowed to roam unsupervised by their owners. In some cultures dogs are accepted as part of the ecology of a community and are rarely considered as being owned by an individual person or household.

Although dogs have many useful and varied functions within human society, their populations may require management to ensure that the size and type of dogs within the population matches the needs of human society, and that dogs can co-habit the environment without undue risk to humans or other animals. This chapter explores the problems

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that can arise from dog populations, and hence motivations for management. It also considers the assessment of dog populations to improve understanding of their dynamics and human attitudes towards them, and how the results of such assessments can be used to develop management programmes that suit both the dog population and the human society in which they live. The potential components of humane programmes are introduced, and, finally, how these programmes can be evaluated to improve performance is discussed.

## Problems of Dog Populations and Motivations for Management

#### Dog population management by owners

Since dogs were domesticated, humans have been selecting preferred individual dogs and providing care to ensure survival of these individuals, and often also to support successful breeding to maintain a population of dogs with desired traits. Concurrently they will have prevented breeding of less preferred individuals, and perhaps even withdrawn resources, or purposefully killed dogs that either physically or behaviourally did not match sufficiently a desired ideal, or when the number of dogs exceeded what was deemed appropriate or possible to maintain.

However, the extent of conscious planning in dog population management on the part of humans can be overestimated. Survival of individual dogs and their offspring is very reliant on the resources made available by people, but the decision to provide these resources may be predominantly a subjectively or emotionally driven decision, as opposed to an objective decision based on some concept of an ideal dog population. For example, the significant role of children in caring for dogs and therefore selecting dogs that will be given care may involve limited consideration of suitability for function. However, it should be noted that traits such as friendliness and playfulness likely to be valued by children are ideal traits in a dog whose future function includes companionship.

The dog owner-mediated control of dog populations may be sufficient to maintain the population of dogs at a tolerable level. In rural situations even those dogs that are not purposefully killed but are abandoned are unlikely to survive for very long, and are extremely unlikely to breed successfully. For example, a population of feral dogs observed in a rural area of Italy in the 1980s was not reproductively self-sustaining and hence could not be maintained without contribution of new individuals from locally owned dog populations (Boitani et al., 1995). Dogs, with some notable exceptions, are not able to survive and breed successfully independent of resources provided by humans (WHO and WSPA, 1990), and hence control mediated by the decisions of individual dog owners may be enough to manage the population successfully. However, the suffering experienced by abandoned dogs and the methods of killing unwanted dogs such as drowning and hanging give rise to animal welfare concerns, and hence the development of humane population management programmes may be needed for ethical reasons.

#### **Carrying capacity**

The number of animals that can survive and breed in any location is determined by the *carrying capacity* of the habitat; the level of resources such as food, water, and shelter needed by each species and available in the habitat. For the domestic dog these resources are predominantly controlled by humans, hence in most locations the vast majority of the dog population must be owned. However, as human populations become dense, so the owned dog population becomes increasingly dense and, especially in urban areas in the developing world, the private property available to each dog is limited. This results in a high density of dogs in both private and public areas, as owned dogs are allowed to roam outside their owner's property. In addition, resources in the form of waste often arise, as disposal systems are overwhelmed; this provides a relatively uncontrolled resource that can be accessed

by all dogs – including abandoned dogs that would not otherwise survive.

One factor that can significantly impact on the number of dogs, but which is often missed when the carrying capacity of an environment is assessed, is human tolerance of dogs. Human attitudes towards animals in general, and specifically their tolerance towards dogs in the environment, can work either to increase the dog population through increased dog ownership and care of roaming dogs, or to decrease the dog population through limiting dog ownership and killing or removing resources from roaming dogs. If the density of the dog population increases, at some point these dogs may be seen as a 'nuisance' to society and either local people or authorities will act to reduce this population, usually through killing. The point at which these dogs become a nuisance will depend on the attitude and tolerance towards dogs. Conversely, in some cultures dogs are not just tolerated on public property but are deliberately fed by people, leading to dog population sizes that seem beyond the capacity of the visible waste resources. It is this

variation in human tolerance that leads to the extremely high density of 'street dogs 'seen in many Indian cities, as compared with the relatively low densities of dogs seen in the cities of countries such as Egypt.

# Defining categories within the dog population

Dog populations comprise different categories of dogs, commonly defined by their ownership status and/or their behaviour. Attitudes towards these different categories of dogs and also methods of managing their populations differ. Figure 11.1 was taken from the International Companion Animal Management (ICAM) Coalition<sup>1</sup> humane dog population management guidance (2008).

The definition of a roaming dog provided by the ICAM Coalition is 'One that is not currently under direct control or is not currently restricted by a physical barrier'. From this definition and Fig. 11.1 it can be seen that a roaming dog, sometimes called a *stray*, *street*,



**Fig. 11.1.** Sub-populations of the total dog population. This diagram shows the sub-populations into which the total dog population can be partitioned. Note that these categories are fluid and dogs may move between categories, as indicated by the arrows.

or free-roaming dog, might actually be an owned dog that is allowed to roam, or a recently owned dog that has been lost or abandoned. The importance of this definition is that it is usually the roaming dogs that are perceived by society to be a problem, and hence a focus for management. In the section 'Understanding dog populations and implications for management' (below) the importance of initial assessment of the situation is discussed, so the dog-related problems faced by society can be scrutinized and the causes of these problems highlighted as the focus for management. This initial assessment should also challenge commonly held assumptions, such as the idea that all roaming dogs are unowned.

An additional sub-category of unowned roaming dogs is *feral* dogs. The definition of a feral dog used by Boitani et al. (1995) is 'a dog living in a wild and free state with no direct food or shelter intentionally supplied by humans (Causey and Cude, 1980), and that did not show any evidence of socialization to humans (Daniels and Bekoff, 1989), but rather a strong continuous avoidance of direct human contact'. Such dogs may be found in rural areas outside human settlements. As discussed in an earlier section of this chapter, the survival and reproductive success of these dogs is limited. Feral dogs have commonly begun life as owned or unowned dogs living within human settlements, and have become feral due to being forced out of the settlement. Notable exceptions include Australian dingoes, which have bred successfully independent of resources provided intentionally by humans for many generations, and, having totally lost any domesticity, are often no longer considered feral (Price, 1984) but rather a wild species of canid. Commonly the number of truly feral dogs that exist in a particular location is overestimated. For example, owned roaming dogs from one village visiting a neighbouring village in response to a female coming into oestrus can be mistakenly termed feral or wild dogs by people in the receiving village. The limited lifespan and poor reproductive success of these dogs also means that if management programmes effectively address the owned and unowned roaming dogs within human settlements, the reduced contribution

of dogs to feral populations will lead to their eventual extinction. In recognition of this, the rest of this chapter will focus on the confined and roaming dogs found within human settlements and relying on resources provided by humans.

As reflected in Fig. 11.1 and discussed in relation to feral dogs, dogs can move between categories within their lifespan. These categories are useful to help understand dog populations, but it must be recognized that the process of moving between these categories will be just as important, and that individual dogs may not move abruptly from one category to another; hence, definitions may become blurred for individual dogs.

#### Problems caused by dogs

Although dogs provide many benefits to society, they can also cause problems to other animals and to humans. These may increase as the dog population rises, but will be most affected by an increase in the proportion of unowned or uncontrolled dogs in the population; for example, under the conditions of dense human populations in urban areas described earlier in the chapter. It is not uncommon for municipalities to quote complaints about dogs as one of the top three concerns reported to the authorities by local citizens.

Problems caused by dogs include (ICAM Coalition 2008):

- Disease transmission to other animals and to people (zoonotic diseases).
- Injury and fear caused by aggressive behaviour.
- Nuisance through noise and fouling.
- Livestock predation.
- Road traffic accidents.

In a recent report, the RSPCA (2010) estimated the annual societal costs of the 10 million dogs living in the UK. These included:

- £3.9 million from dog bites leading to hospitalization.
- £2.8 million from injury to or killing of livestock.
- £14.6 million from casualties in road traffic accidents involving dogs.

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The UK is currently free of rabies and *Echinococcus*. The costs of control and treatment of zoonotic diseases related to dogs will be far higher in countries where these two diseases are endemic.

#### Problems encountered by dogs

The problems caused by dogs are clearly a priority for authorities; however the problems encountered by dogs are also important and can make up a significant proportion of the dog-related complaints reported by local citizens.

Both owned and unowned dogs can suffer from malnutrition, diseases such as mange and distemper which cause visible distress, injuries through fighting and road traffic accidents, and abusive treatment from people. Attempts to control the dog population by authorities can also cause welfare problems including inhumane methods of killing such as strychnine poisoning, electrocution, shooting, clubbing, and drowning; cruel methods of catching such as those using metal tongs and uncovered wire nooses; and poorly equipped and managed holding facilities. Even if the practices involved in control methods are improved to ensure any potential animal suffering is minimized, the number of dogs humanely culled due to lack of available homes may be seen as an unacceptable wastage of life. In the United States, the number of dogs and cats euthanized in government and non-governmental centres is estimated by the Humane Society of the United States as between 3 and 4 million per year (HSUS, 2009), although this is a significant improvement from their estimate in 1973 of 13.5 million dogs and cats euthanized (Scarlett, 2004). This is widely considered as unacceptable to US society and as a result significant investment is made in dog population management to reduce this unwanted or 'surplus' dog population.

#### Dog welfare and humane management

The welfare of an individual animal relates to its ability to cope with the challenges presented by its environment. If the environmental challenges overwhelm its ability to cope then the animal may suffer both physically and mentally (adapted from Broom, 1986). One framework commonly used to measure the welfare of an animal is the *five freedoms* (FAWC, 1979), which suggest animals should have:

- Freedom from hunger and thirst.
- Freedom from discomfort.
- Freedom from pain, injury, and disease.
- Freedom to express normal behaviours.
- Freedom from fear and distress.

Measuring these will provide an assessment of an animal's welfare on a scale from 'very good', where all freedoms are achieved, to 'very bad', where none are achieved.

The extent to which people are responsible for the welfare of an animal will depend on the situation. In the case of domestic animals, people have artificially selected for certain traits to suit human requirements, and this has altered the ability of these animals to cope with the environment. As such the welfare of domestic animals is clearly a human responsibility. Legislation relating to animal protection commonly states that the responsibility to ensure a reasonable level of welfare of owned animals is a legal obligation of owners, sometimes termed a 'duty of care'. Similarly, with any animal (wild or domesticated), when the activity of humans impacts directly on the animal for example, if this animal is being kept in captivity - its welfare is the responsibility of humans and should be maintained at the highest possible level. As Mahatma Gandhi said, 'The greatness of a nation and its moral progress can be judged by the way its animals are treated."

In the case of dog population management, dog owners have a moral (and sometimes legal) imperative to ensure their dog experiences a reasonable level of welfare. Similarly, if population management interventions are used, these should be conducted humanely to minimize any potential suffering for the dogs involved. Using inhumane methods of management is not only unethical and potentially illegal, it is also likely to be rejected by local citizens, and, as their involvement in any intervention is necessary for effective control (see Section 4), this can also lead to failure to control the dog population.

#### Summary

Dogs provide many benefits to society but they can also cause problems to humans and experience welfare problems themselves. Owner-mediated control of populations can become overwhelmed, in particular in situations of dense human populations, and hence additional interventions to help manage populations may become necessary. When management is needed it is ethically appropriate that this is done humanely to minimize the problems encountered by dogs, as problems caused by dogs are concurrently reduced.

# Understanding Dog Populations and Implications for Management

#### Suitability to local conditions

Dog populations in each location will vary in important ways that affect how they should best be managed, including their function and human attitudes towards dogs. The perceived problems that dogs present to society will also vary. Is there a zoonotic disease, such as rabies, that distresses people? Is it simply that there is a perception of too many dogs on the streets? Is the major concern the poor welfare of dogs resulting from inhumane control? Once the problems caused by and encountered by dogs are identified, the causes of these problems can be explored, and a management programme can be designed to suit the location.

A common mistake made in dog population management is that this initial step of understanding the situation objectively is not attempted. Instead, a style of population management that has worked in a different location is simply imported, on the assumption that it will work anywhere. In reality there is no single method of population management that is guaranteed to work in all locations.

The cost of dog population management can be significant and is not a short-term challenge but a permanent requirement, as it can be assumed that a proportion of people will always choose to own dogs, and hence there will always be a population of dogs that require management. In the United Kingdom, the RSPCA (2010) estimated the annual cost of enforcing dog welfare laws and kennelling, reuniting, and re-homing stray dogs as totalling nearly £100 million, more than double the estimated societal cost of dogs including dog bites, livestock predation, and road traffic accidents. This cost of dog management is considerable and it is essential that interventions to manage populations are designed carefully to ensure the best use of funds.

# Who is responsible for dog population management?

As stated in the ICAM Coalition humane dog population management guidance (2008),

responsibility for dog population management properly resides with local or central government. Animal welfare NGOs should not be encouraged, nor seek, to take on the authority's overall responsibility for dog population management other than through a contractual agreement, with appropriate funding and resources.

NGOs (non-governmental organizations) can, however, support governments in the development of suitable strategies for dog population management, and contribute to an overall management strategy by providing specific services most suited to their capacity, such as education, rehoming, and low-cost veterinary services.

Perhaps the most important stakeholders in dog population management are the dog owners themselves. As discussed above, dog owners can manage dog populations themselves to a certain extent, but they will require the support of certain professions, not least the veterinary profession (which has a very important role in population management) to do this well and humanely. Dog owners can also contribute financially to dog population management through dog licensing systems (see further discussion in 'Understanding Dog Populations and Implications for Management', below).

Although governments hold the majority stake in running and financing dog population

management, many other stakeholders should be involved. To encourage the participation of relevant stakeholders, a multi-stakeholder committee can be created to assess the situation, design and implement an appropriate management programme, and evaluate it to improve performance. These stakeholders may include (ICAM Coalition 2008):

- Government.
- Veterinary community.
- NGO community.
- Animal sheltering, fostering, and rehoming community.
- Academic communities with relevant experience, e.g. animal behaviour, veterinary science, sociology, ecology, and epidemiology.
- Legislators.
- Educators.
- Local media.
- International bodies with relevant responsibilities.
- Local community leaders/representatives.
- Local community, including both dog owners and non-owners.

#### Exploring the 'problem' and its 'causes'

The first step for an assessment that will lead to designing a dog population management programme is to establish the dog-related problems experienced by the community in the location in question (see 'Problems caused by dogs', above, and 'Interpretation of Data', below). This is where the benefits of a multi-stakeholder committee begin, as each stakeholder will provide a different perspective on these problems. Once the priority problems have been identified, each problem needs to be explored to understand its causes, essentially asking the question 'why does this problem exist?'

The following are examples of identified problems and questions that could be used to explore their causes:

• The problem of rabies transmission to people and livestock has been identified as a priority for a certain town. The question is what causes this unacceptably high

incidence of rabies. Finding the causes will focus the future management programme. The following are just some of the questions that need to be answered:

- Are there particular categories of dogs that are over-represented in the dog rabies cases? Is surveillance of animal and human rabies cases sufficient to provide a meaningful picture of rabies incidence?
- Why are these dogs not vaccinated against rabies? Do people not understand the importance of vaccination? Are there vaccines accessible at a reasonable cost? Can these dogs be accessed for vaccination?
- Are there any other reservoir species for rabies?
- Is the virus circulating within the current location or is it being imported from other places?
- Do people know what to do if they are exposed to rabies? Are certain people more at risk of being bitten? Are the hospitals and health centres equipped to provide the correct treatment?
- The problems of road traffic accidents caused by roaming dogs and the suffering of injured or diseased roaming dogs have been identified as priorities for a city. Possible questions to identify the cause or source of the roaming dogs include:
- What is the current size of the dog population and the categories within it? This includes both owned and unowned, confined, and roaming dogs, and where these overlap.
- Where are the roaming dogs coming from? What are the sources of these dogs and why do these sources exist? Are these owned roaming dogs or abandoned dogs, or are unowned dogs breeding successfully in this city and producing the next generation of roaming dogs?
- What are the main welfare issues faced by these dogs? What diseases and injuries are they suffering from?
- Are there particular areas of the city where these problems are worse?
- For a particular region, the priority problem has been identified as an overwhelming number of dogs being abandoned by owners to shelters, leading to

overcrowding and hence poor animal welfare, or avoidance of poor welfare by culling large numbers of dogs. Questions include:

- What age and type of dogs are being abandoned by owners? Puppies or adult dogs? Certain breeds or types of dogs?
- Why are dogs being abandoned by their owners? Is it because of unwanted litters? Did their expectation of dog ownership turn out to be incorrect? Do many of these dogs have 'behaviour problems'?
- What is the rate of adoption from shelters? Why do people choose to adopt and why would they choose a different source for acquiring a new dog?
- Where do most people get their dogs from? Adoption? Gifts from other people? Bred themselves? Purchased from breeders or pet shops?

For each problem an additional question should be asked about what is currently being done, both informally and officially, to control the dog population. It is important to learn from current and past control measures to establish what has worked and what has failed. Similarly, learning from other locations can be very useful, but this must be done with awareness of suitability to the current location, taking heed of the points discussed earlier under 'Suitability to local conditions'.

#### Methods for investigating key questions

There are several different methods or tools that can be used to investigate the dog population and human attitudes and behaviours related to dogs, in order to answer these key questions:

#### 'Street' surveys of dog populations

Street surveys of dog populations involve direct observation of roaming dogs on public property following a clear protocol to ensure repeatability. These surveys can estimate or monitor the number of roaming dogs in public areas at a particular time (available on the tools and resources page of the ICAM Coalition site<sup>2</sup>). Establishing a reliable estimate of the number of roaming dogs is useful, as estimates based on community perceptions or even official statistics can vary wildly, and are commonly overestimated. For example, a population survey of Cairo completed for WSPA by Conservation Research Ltd in 2006 (unpublished data) provided an estimate of approximately 25,000 roaming dogs in Cairo with a maximum upward bound of approximately 50,000. This was a significantly lower estimate than given previously by local media and authorities of 2 million roaming dogs. Surveys can also provide information on the welfare status of these dogs, by using basic measures such as body and skin condition; and of reproductive activity, by measures such as the percentage of lactating females. By selecting survey methods that are reasonably cost- and time-efficient, surveys can be repeated at regular intervals to provide a measure of changes in reproductive activity, welfare, and population size over time.

#### Focus groups/informal interviews

Interviews can be defined as 'informal' when open-ended questions are asked to a group of people and the questioning is allowed to develop as a conversation, as opposed to following a strict script of predefined questions. The aim of focus groups and informal interviews is to explore the subject area from a range of different perspectives, so it is important to ensure that a good representation of the public is included. The composition of the groups should be carefully considered to ensure everyone feels relaxed and able to respond and discuss the subject matter openly and honestly with the interviewer. This may mean that a mixing of genders, ages, and socio-economic groups may not be suitable, although they should all be represented across the groups.

#### Questionnaires

Questionnaires tend to use structured questions, delivered by an interviewer in person, over the phone, or online, to establish quantitative information. The information is hence reliable and repeatable but can be considered 'shallow' in comparison to that gathered through focus groups and interview. It is common to start with focus groups and informal interviews to gather in-depth information, and then to design a questionnaire if there are particular areas for which quantitative information is required. For example, a questionnaire is a good way to establish the number of dogs each household owns, the proportion of households that own a dog, and the gender of these dogs; a focus group or informal interview is a good way to explore why people choose to own a dog and why they may choose a male dog over a female.

# Knowledge attitude and practice studies

Knowledge attitude and practice (KAP) studies are a form of questionnaire usually delivered via face-to-face interviews with individuals or small groups. The questions themselves may be either closed or open-ended and hence allow for a greater depth of information; however, these questions are designed to be focused on the knowledge the person or group has about a specific subject, their attitudes towards this subject including any preconceived ideas, and practices as reflected by their actions relating to the subject.

#### Example: Colombo initial assessment

Colombo is the capital city of Sri Lanka and until 2006 controlled its dog population by catching roaming dogs in response to public complaints, and killing them in the municipal pound, usually by inhalation of exhaust fumes. The Colombo Municipal Council (CMC) was motivated to find a more effective and more humane way of managing the dog population. In collaboration with the CMC, an initial assessment of the situation was completed in mid-2007 by WSPA and a local NGO, the Blue Paw Trust, to design a management programme for the city. The priority problems identified were a persistent level of dog and human rabies cases, and complaints from the public about nuisance behaviours of roaming dogs and the poor welfare of some roaming dogs.

The assessment consisted of two related elements: (i) a direct observation survey of

roaming dogs in the early morning (peak time for roaming dogs in Colombo), and (ii) a questionnaire of dog owners and non-owners. Both the survey and questionnaire were carried out in a sample of eight wards (17% of the 47 wards in the CMC), involving the direct observation of 625 roaming dogs, 275 owned dogs, and a total of 1823 households (8% of households from the sample wards) in the survey. The aim was:

- to estimate the size and composition of the entire dog population in the city (both roaming and confined dogs);
- to investigate the welfare status of these dogs;
- to begin to understand the dynamics of the population;
- more specifically, to learn what was maintaining the roaming dog population;
- to establish the true vaccination coverage of the dog population;
- to learn which dogs were not being vaccinated.

Following informal interviews to create a better understanding of dog ownership and attitudes in Colombo, a questionnaire was designed to cover subjects such as the number of dogs owned by each household, and the number and fate of dogs that had left the household over the last 12 months, with responses to statements relating to dogs (including sterilization and killing) recorded on Likert scales from 'strongly agree' to 'strongly disagree'. Finally, the body and skin condition of any and all owned dogs currently visible in the household were recorded, and the owner was asked whether these dogs were allowed to roam outside their property in the early mornings. The direct observation survey and count of roaming dogs included all dogs seen on public property and not currently under the control of an owner. For each dog observed, the following information was recorded:

- gender;
- age (split into puppies below 4 months old, and adults);
- if female, whether lactating or not;
- body condition score on a 5-point scale; and

• the presence or absence of a visible skin condition (this was the same scoring system as used for owned dogs in the questionnaire).

The results of this assessment are discussed in 'Example: Colombo interpretation', below.

#### Interpretation of data

#### Principles

Utilizing methods for investigating the dog population can create a large body of data. The next stage is to interpret these data in order to answer the key questions and hence inform the design of the management programme. Again, a multi-stakeholder committee can be beneficial, as interpretation will usually profit from a range of perspectives.

It may be helpful to structure these interpretation discussions starting with a summary of the data collected using each method, and then working systematically through the key questions that were previously identified as important for establishing the cause of the problems. For each question, the relevant data can be highlighted and used to establish an agreed answer. An alternative is to structure the discussion by working through a series of important 'factors', such as those identified in the ICAM Coalition humane dog population management guide. These are factors likely to be common to all dog populations and can be used to cluster the data into manageable subjects for discussion:

- Human attitudes and behaviour relating to dogs
- As discussed previously, the survival and reproductive success of dogs is reliant on resources provided by people. Consequently, human attitudes towards dogs and their behaviour relating to dog care and tolerance of roaming dogs, is likely to be the most powerful force behind dog population dynamics and the welfare of dogs.
- The data collected plus input from members of the committee can be used to answer questions such as: what do

people think about dogs in this location? How do they treat dogs? Do they provide care to their own dogs?

- Reproductive capacity of dogs
- Ideally the number and type of dogs that exist should match what is wanted and manageable by the local community; 'supply should match demand'. But this is commonly not the case, leading to a population of unwanted dogs that may be abandoned or killed.

Data and committee input can be used to answer questions such as: are there particular categories of dogs that seem to be reproducing most successfully? Are there particular categories of dogs whose puppies are most likely to be unwanted?

- Is there commercial breeding and selling in this location? What are the standards/ regulations relating to this trade, and what is the welfare of dogs produced by this trade?
- Access to resources
- Resources including food, water, and shelter may be provided by an owner within a household or available on public property. The extent to which a dog relies for survival on resources available on public property will depend on whether it is owned, and the level of care provided by its owner. Restricting access to resources on public property will discourage opportunistic roaming and scavenging of owned and fed dogs. However, it may also reduce the survival of those that depend on these resources, so this should be done with care, and the impact on local populations should be monitored to ensure that animals are not starving as a result.

 Data and committee input can address questions such as: are dog owners feeding their dogs regularly, or are they likely to be reliant on other food sources? What food sources exist in the local community? Are the dogs feeding on these resources reliant on them for survival? Are there particular areas in the local community where roaming dogs are not tolerated (e.g. hospitals and schools) that could be targeted to change the dog population in a localized way?

- Zoonotic diseases
- Zoonotic diseases are often the primary cause for concern with regard to dog populations, particularly for local and central governments, which have a responsibility for public health. Because rabies is a fatal disease, and dogs are the most common vector for transmission to humans, rabies control is often a major motive for dog population management. Other diseases such as Leishmaniasis and Echinococcus may also be relevant.
- 0 Data and committee input can address questions such as: what zoonotic diseases exist in this location, and what are the trends in their incidence? Are particular categories of dogs over-represented in the case load? What methods of prevention exist for these particular diseases (vaccines, de-worming, vector repellent) and what is the availability of these methods in this location? Are dog owners using these preventative measures, and if not, why not? Are there precautions that staff working on the future management programme should take to prevent transmission of zoonoses?
- Current roaming dog population
- This population can lead to humananimal conflicts in addition to zoonotic diseases, and can have visible animal welfare problems. In many situations this population will need to be addressed for reasons of public pressure, public health, and the welfare of the animals themselves. The best method of doing so will depend on the human community and the dog population itself.
- Data and committee input can address questions such as: what are the sources of roaming dogs? Where do they come from? What is the roaming dog population size in the location, and how is this split between different categories? Are there particular areas where density of roaming dogs is high, and if so, why? What is their welfare state? How do local communities treat them? How do people feel about them? Would they adopt a roaming dog from the street or from a shelter?

Finally, data and committee input can be used to answer questions regarding the control measures used to date. What has worked, and what has failed? What can we learn from other locations?

### Example: Colombo interpretation

Using the results of the initial assessment introduced in 'Street' surveys of dog populations', above, the following interpretations of the dog population were drawn from the data for the CMC area of Colombo.

WHERE ARE THE ROAMING DOGS COMING FROM? IN some areas many of the roaming dogs encountered appeared to be unowned, both because of the lack of dogs with body condition scores over 1 or 2 (scored from 1 to 5), and also the behaviour of most dogs when approached was to move away, rather than to move into private property or attempt to defend a threshold. The questionnaire results confirmed this impression that the percentage of roaming dogs that are owned is low in some areas, but also that overall, around 50% of roaming dogs are actually owned dogs. Owners reported that 25% of the owned dog population was allowed to roam unsupervised. Nearly three-quarters of all respondents said that if they had a female dog that had puppies, they would not want to keep them; a similar response was also given by those respondents who in fact did own one or more female dogs. However, there were actually a relatively low number of litters reported by the dog-owning households, suggesting that much of the pup production maintaining the unowned population may be occurring outside the dog-owning households, presumably with local people providing some support to unowned females with litters. Despite seeing 11% of the roaming females lactating, there was a low percentage of pups (7%) seen on the street, suggesting that the roaming population cannot be sustained entirely by survival of pups born on the street. In conclusion, the roaming dog population seems to be maintained by a combination of breeding on the streets by unowned dogs, abandonment of unwanted dogs (perhaps particularly female dogs and their offspring), and owners allowing their dogs to roam.

WHAT WELFARE PROBLEMS ARE THE DOGS SUFFERING FROM? A greater percentage of roaming dogs (42%) suffered from skin conditions as compared with owned dogs (17%). There was some suggestion from the informal interviews that people were concerned about catching skin conditions from dogs, hence skin conditions in owned dogs may have led to abandonment. Only 29% of owned dogs were never treated for ectoparasites, and 43% were only treated infrequently. The responses to the 'attitude' questions suggested that the care provided to dogs was related to the attitude towards them, with dogs belonging to people with a less positive attitude being less likely to be vaccinated and dewormed, and more likely to suffer from skin conditions. Body condition scores were slightly worse for roaming dogs (32%) with scores of 1 or 2, reflecting emaciated or thin body condition) than for owned dogs (27% with scores of 1 or 2).

ARE PARTICULAR CATEGORIES OF DOGS OVER-REPRESENTED IN THE RABIES DATA? Of the owned dogs, 88% were reported to be vaccinated, although only 83% in the previous year. This suggested that the unowned dog population, and perhaps also owned puppies prior to vaccination, were the most likely to act as a reservoir for rabies.

ATTITUDES TOWARDS DOGS AND METHODS OF CONTROL The majority of respondents said that the welfare of street dogs was important to them, with dog owners seeming to have a more positive attitude than nonowners. In addition, 77% of dog owners suggested they could handle dogs other than their own. However, few people liked having dogs around on their street and most agreed that street dogs pose a danger to people and should not be allowed to breed. However, 78% of respondents believed that it is not acceptable to kill dogs. This provides support for the need for an effective and humane intervention that addresses the source of roaming dogs and so avoids the

need to remove them. People were also willing to adopt roaming dogs with 'adopted off street' being the third most common source stated for owned dogs. This seemed to be particularly the case for male dogs, contributing to the 1:1.8 ratio of females to males in the owned dog population.

FROM INTERPRETATION OF DATA TO PROPOSED METHODS OF MANAGEMENT The interpretation of the data suggested that to effectively manage the dog population for the long term a comprehensive and humane programme would be necessary. This would need activities to achieve the following:

- To reduce reproduction in the dog population including both owned dogs where puppies were not wanted, and unowned dogs.
- To improve responsible dog ownership to increase care and hence improve the welfare of dogs.
- To reduce abandonment and the unsupervised roaming of owned dogs.
- To build on the current inclination to adopt.
- To increase rabies vaccination of unowned dogs.
- To manage areas where roaming dogs are not well tolerated.
- To respond to sick, injured, and aggressive roaming dogs in a humane and effective way.

One of the proposed elements was surgical sterilization of dogs. Initially this would be carried out through encouraging owners to bring dogs for sterilization, hence also providing the opportunity to promote and support responsible dog ownership practices. The impact of this on the roaming dog population would depend on how many roaming dogs are brought for sterilization, and the survival of pups born to unsterilized roaming dogs. The programme would explore ways of building on the current level of concern for roaming dog welfare and feeding already commonly offered to these dogs by local people. It would encourage people to take a further step and take responsibility for getting roaming dogs sterilized and caring for their health, even if they are currently considered unowned.

#### Summary

Taking the time to investigate the dog population and how local people feel and behave towards the dogs will lead to greater understanding of dog population dynamics, the problems created by the dog population and experienced by the dogs themselves and also perhaps most importantly why these problems may exist. From this position of greater understanding, the design of the population management programme will be significantly improved and hence successful and sustainable management of the population will be more likely. Development of a multi-stakeholder group to complete this stage of investigation and interpretation is likely to be very beneficial and this same group should be prepared and motivated to move to the next stage of programme design and implementation.

# Components of a Comprehensive Humane Dog Population Management Programme

A dog population management programme can be designed to suit the location, based on an understanding of the dog population and the attitudes and behaviour of the local human community towards dogs, as discussed above. A number of components or activities that complement each other are likely to be required to form a comprehensive programme. The sustainability of each component will be a relevant consideration even at the outset, as it must be realized that dog population management is not a short-term challenge but a permanent requirement for society. However, these components will need to evolve over time, in step with changes in dog population dynamics, ownership, and attitudes towards dogs. In this section a range of common components is described, with the likely aim in using each, and some examples from different countries.

#### Education

Human behaviour towards dogs is such an influential factor with regard to dog welfare,

survival, breeding, and where and how they live that education of people is similarly an influential component of dog population management. Education messages and delivery need to be targeted towards specific audiences and developed and delivered with support from education specialists. Target audiences and the aim of education efforts will probably include the following:

- Dog owners. The aim of educating dog owners is primarily to increase responsible dog ownership to improve dog welfare, to reduce potential disease risks through owners investing in preventative measures such as vaccination and parasite control, and to improve approaches to dog acquisition and retention, reproduction, and rehoming.
- Children. Children are commonly closely involved in dog care, and hence one aim will be to improve their responsible ownership behaviour as described in the previous point. However, children are also commonly over-represented in the dog-bite data, so an additional aim is to improve their behaviour in interactions with dogs and reduce bite incidence.
- Veterinarians. Veterinarians are key professionals who should be engaged and involved in dog population management. They are often considered the primary source for information about dog care by owners, and have a clear role in providing disease prevention measures, dog health care, and dog reproduction control. The aim in educating this audience is to build its knowledge and engagement in dog population management by supporting the development of key skills such as surgical sterilization, humane methods of euthanasia, and knowledge of the impact of dogs in public health.

 Animal Control Officers (ACOs). ACOs may have different titles according to their country and their responsibilities. This profession is at the 'front line' of dog population management and usually responsible for responding to complaints about dogs, enforcing dog-related regulations, and talking to the public about its responsibilities. The aim in education of this audience is to equip ACOs with the knowledge and skills they need to humanely handle and care for animals they become responsible for, and to communicate responsibly and accurately with the public about its responsibilities, including dog care.

#### Example: ACO training, Brazil

In many countries, ACOs represent an undeveloped profession and the staff employed to fulfil these roles have had minimal prior training or support, so their handling techniques and attitudes commonly lack respect for animal welfare or for their potentially influential position in the local community. It is not uncommon for the behaviour of these staff towards animals and the public to be a source of public complaints and animosity. In recognition of this challenge in Brazil, the Institute of Education and Population Management (ITEC) developed a course for ACOs. The ACOs from several Zoonosis Control Centres are brought together for 1 week for a series of lectures, activities, and technical training sessions. The strength of this course is that it not only provides training in technical skills and knowledge of subjects such as zoonosis control, but also addresses attitudes towards animals, and empowers the ACOs to recognize the contribution they can make to animal welfare and human health. The aim is to change the behaviour of the ACOs towards animals and the public, and for them to become champions for animal welfare and humane zoonosis control, as opposed to - at times - a source of animal cruelty. The impact of the course on each ACO can be considerable, as this may be the first time they have been provided with training and empowered to have respect for themselves and what they can offer to the public health and to animal welfare. Observed impacts at the Zoonosis Control Centres have been:

- a change from inhumane methods of culling to humane methods;
- commencement of sterilization services at the centres;
- improved welfare of impounded animals;

- an increase in adoption of dogs from the centre; and
- a reduction in catching of dogs due to an increase in the use of owner education to reduce numbers of roaming dogs, as opposed to catching roaming dogs without speaking to owners.

#### Legislation

As previously discussed, dog population management is a permanent challenge for society and so should be well supported by legislation at both central government level to maintain minimum standards, and at local government level to allow variation in management styles according to the location. Legislation should aim to cover several areas:

Protection of animals from cruelty. Animal owners and people temporarily responsible for animals have a 'duty of care' to maintain a reasonable level of welfare, by ensuring animals are provided with the care necessary to meet their needs. The Five Freedoms introduced earlier in this chapter can be used as inspiration. The UK Animal Welfare Act 2006, for example, includes legal obligations to provide a suitable environment, food, and housing; allowing the animal to exhibit normal behaviours; and protection from pain, suffering, injury, and disease. In addition to this legal framework, additional 'codes' can be written for different species, including dogs, to provide owners with more information and guidance as to what suitable care entails. For example, in New Zealand the Dog Code<sup>3</sup> provides both minimum requirements and also best practice guidelines for dog care. Methods of killing animals by owners, professionals such as vets, and authorities responsible for animal control can also be included to protect animals from cruelty. Hence the use of poisons such as strychnine, which cause significant suffering, and physical methods, such as drowning and electrocution of conscious animals, would be forbidden

in this section of the law. This section can also stipulate reasons why animals should be killed, for example owners have a responsibility to treat or euthanize their animal if it is suffering. Some countries have chosen to introduce legislation that forbids the killing of healthy dogs. While this should be the longterm goal of society, introducing such legislation when humane and effective methods of reducing the unwanted dog population have not yet been developed is likely to lead to significant animal suffering in shelters and on streets, and considerable cost to society in housing dogs and treating zoonotic diseases.

- Dog control laws. The requirements for local authorities to provide dog population management capacity, including suitably skilled staff to fulfil designated roles, and infrastructure such as holding facilities, should be covered in this section. This may also include additional regulations relating to zoonotic control and in particular during 'outbreak' situations.
- Dog registration, identification, and licensing. These may be included with dog control laws, and relate to both owner and authority responsibility to ensure dogs are identified, registered on an accessible register, and, if relevant, licensed and any fees paid. Registration and identification provide a link between an owner and their dog, legally and sometimes visibly (dependent on the method of identification: microchips, for example, are not visible but owners may also be required to ensure their dogs are collared and tagged). Hence this both encourages responsible behaviour and provides a basis for enforcement of other aspects of legislation. Identification and registration also provide a fast way to reunite dogs with their owners should they become lost. With this in mind, national databases should be used and linkages between national databases built for animals that move between countries. It is also essential that the process of updating owner information such as change of address or ownership is fast (preferably

completed online), to ensure information remains up-to-date, and that the data are accessible. Licensing of dogs involves the payment of an additional fee, usually annually. Benefits of licensing include:

- an income that can be used to support dog population management programmes following the 'polluter pays' principle by putting the cost of dog population management primarily on dog owners rather than the general public;
- differential licensing fees to encourage responsible behaviour such as neutering or adoption of dogs and allowing free licensing for assistance dogs and lowincome owners; and
- encouraging an annual check of registration details to help keep information updated.
- The fee for licensing a dog and penalty for failure to license needs to be set with care. Too high, and owners will be forced to abandon dogs; dog ownership will become unaffordable for lowincome people who may well rely on their dogs for security or for protecting livestock; and people will be discouraged from adopting or caring for roaming dogs. Too low, and dog owners may see licensing as irrelevant, or the cost of running the licensing system will not be covered, leaving no additional funds for dog population management activities. Switzerland has also adopted a compulsory training course for dog owners, and basic training for all dogs, as part of the requirements for dog licensing to help improve responsible ownership, animal welfare, and reduce the incidence of behaviour problems that commonly lead to abandonment. The impact of this scheme is yet to be established.

 Control of the supply of dogs. Commercial breeders and sellers should be subject to regulations that ensure the welfare of the animals involved is protected. This should include a minimum age at breeding, frequency of breeding, and maximum number of litters. Regulations relating to the protection of animals will also be relevant and there will be additional care requirements for pregnant females, nursing mothers, and young puppies. Pet shops and markets should also be regulated to ensure protection of animal welfare and responsible selling practices, including a minimum age for people purchasing animals and a requirement to provide information relating to animal care, for example a copy of the Dog Code if one exists in the country.

Legislation will be a 'paper exercise' unless it is enacted uniformly and enforced effectively. Effective enactment will usually require the majority of effort to be spent on education and incentives and the minority to be spent on carrying out punitive enforcement measures. Education about legislation has to be targeted at all levels, from law enforcement bodies (such as lawyers, police and animal welfare inspectors) to relevant professionals (such as veterinarians and shelter managers) and dog owners.

Successful enforcement has been achieved in some countries through the use of ACOs (also referred to as animal welfare inspectors or wardens). These officials are trained and resourced to provide education; handle animals when required; and enforce legislation through advice, warnings, cautions, and eventual prosecutions (ICAM Coalition, 2008).

#### **Reproduction control**

The aim of reproduction control is to help reduce the unwanted dog population by limiting unwanted reproduction in order to match the supply of dogs with the demand for dogs. An additional aim may be to reduce sexual behaviours that are perceived to be a nuisance, such as the ganging of males around a female dog in 'heat' leading to fighting between the males; or to reduce the increased disease risk to dogs presented by mating such as transmissible venereal tumours. Any services provided to help with reproduction control will need to be sustainable and affordable, hence every effort should be made to develop these services locally with the local veterinary capacity, and to encourage owners to perceive

these as valuable services that they should pay for. Ensuring good dog welfare also involves additional ongoing health care needs. In the long term, the dog population will benefit from investing in local veterinary services and matching these with a dog-owning community that values veterinary care, and which does not assume it should be a free service.

There are three main ways that reproduction control can be achieved (ICAM Coalition, 2008):

- Surgical. The removal of reproductive organs under general anaesthetic ensures permanent sterilization and can significantly reduce sexual behaviour (especially if performed early in an animal's development). A good standard of asepsis (the practice of reducing or eliminating the risk of bacterial contamination) and pain management must be maintained throughout. This can only be assessed by adequate post-operative monitoring during the whole recovery period. Surgery may be costly initially, but is a lifelong solution, and hence may be more cost-efficient over time. It requires trained veterinarians, an infrastructure, and equipment.
- Chemical or immunological sterilization or contraception. These methods are still limited by the cost, the fact that they may need to be repeated, and by the welfare problems associated with certain chemicals. Currently, no methods of chemical or immunological sterilization or contraception are guaranteed to be effective or without risk when used on roaming, unmonitored dogs. However, this is an active area of research, and effective and suitable chemical or immunological sterilants for mass reproductive control are expected in the near future. Most sterilants or contraceptives require trained veterinarians for clinical examination (especially to assess the reproductive status of females), prior to the application and administration of injections at regular intervals without interruption, which is not possible for most dog-management programmes. Chemical or immunological sterilants and contraception should

be used according to manufacturers' instructions. They may or may not have an impact on sexual behaviours.

 Physical contraception through the isolation of females in oestrus from entire males. Owners can be educated to recognize the signs of a female dog coming into oestrus, and can plan to ensure the female is isolated from entire males during this period. Attention must be paid to the welfare of both the female and males when this is planned. Sexual behaviour can become problematic, as males will try to gain access to females. However, isolation requires minimal cost to achieve and does not require a trained veterinary surgeon.

The managers of a programme that includes sterilization should ensure that good standards are maintained, regardless of the mode of sterilization used (surgical, chemical, or immunological). This will require prior training of staff and regular refresher training. Staff should also perform consistent follow-up of cases in order to help identify problems and raise/maintain standards. High throughput interventions with large numbers of dogs being sterilized per day can reduce costs, but a weakening of standards must not be allowed.

A common question posed if this component is to be used is: 'What proportion of the population should be sterilized?' Earlier in this chapter, the importance of understanding the problem and causes was discussed, so the answer to this question will depend on the aim of the programme. If the problem is poor rabies control and there is a particular sub-population of dogs expected to produce offspring that will not be vaccinated, the proportion of the total population that should be sterilized may be low. If the problem is abandonment of unwanted females and their litters at shelters, in particular from a certain type of dog, the proportion of the total population may again be low, but high for this particular type of dog. However, if the goal is to stabilize or reduce the total dog population, the following is a useful guide to establish the required sterilization proportion for a desired rate of change. Note that this equation assumes a closed population

by not including the factors of immigration and emigration:

Where
AdultSurv = adult survival
JuvSurv = juvenile (first year) survival
F = fecundity (number of litters per female
per year)
L = average number of females per litter

Sterile = proportion of sterilized females r = rate of population growth

If there is no sterilization of females the rate of population growth is:

r = AdultSurv + JuvSurv F L

If there is sterilization of females, the statement needs to include a factor that accounts for the fact that part of the population cannot reproduce:

$$r = AdultSurv + JuvSurv F L (1 - Sterile)$$

Hence the proportion that needs to be sterilized for a desired r is:

Sterile = 1 - [(r - AdultSurv) / (JuvSurv F L)]

However, people rarely know the adult survival, juvenile survival, or fecundity of their population before they begin (WSPA have tended to estimate these parameters from the data produced by programmes once they have begun). In addition, our experience is that this equation is too simple and belies the complexity of dog population dynamics, and the differing survival and fecundity of the various sub-populations. If the intervention misses a particular sub-population the impact on the population rate can be surprisingly different from the one expected. So an additional important factor is *targeting* of particular subpopulations of dogs, for example female dogs, which are very likely to be the limiting factor for population growth (sterilizing a percentage of females will usually have more impact than sterilizing the same percentage of males); dogs owned by low-income owners who are less likely to be able to afford to keep an unplanned litter; and roaming dogs. By effectively targeting sterilization services towards those dogs that have been identified as important causes or sources of the problem, the percentage that needs to be sterilized can be limited.

How to access dogs for sterilization will depend on the dog population dynamics and human attitudes and behaviours towards dogs, as discussed earlier. In some locations roaming dogs can be caught on the street by dog-handling staff, sterilized, vaccinated, and released (see 'Catch, neuter, and return', below, for more details). In other locations owners can be encouraged to bring their dogs for sterilization at a central point (which can be moved if using a mobile clinic), and additional help from dog handlers with suitable transport might be offered for owners who would struggle to bring the dogs themselves (WHO and Bill and Melinda Gates Foundation, 2009). The relationship between dogs and humans, and hence the ownership status of roaming dogs, can be considered along a spectrum with the following two countries exemplifying the opposite ends of this spectrum (although this has not been the subject of empirical study to date, and is based only on the experience of WSPA):

- In India there is a high level of provisioning for roaming dogs by a sympathetic public, but the sense of responsibility towards individual dogs is apparently low. At the risk of generalizing for a country that includes significant variation between locations, an example may be a family who feeds a specific roaming dog with leftovers every day, the dog plays with the children, sleeps on the doorstep of the house, and may even have a name – but the dog is not considered the property nor responsibility of the family and will not be brought to a central point for sterilization or vaccination. Note that the level of responsibility shown towards a dog that is considered owned, usually a breed-specific dog that is confined on private property, is significantly higher. Hence the proportion of roaming dogs that are effectively unowned is high.
- In Tanzania there seems to be a relatively strong sense of responsibility towards owned dogs, although they are often kept unconfined, there is very limited purposeful feeding of roaming dogs, and minimal refuse available for scavenging

dogs due to home burning of refuse. There is also some anecdotal evidence that when a dog is no longer wanted it is re-homed or killed by owners instead of abandoned. As a result, the majority of roaming dogs are owned.

Because of the differences in the ownership status of roaming dogs, the mode of sterilization (and rabies vaccination) delivery differs. Due to the high proportion of effectively unowned roaming dogs in India there is a predominance of the use of catch, neuter, and return (CNR) (see 'Catch, neuter, and return', below). Roaming dogs are caught by dog-handling teams, and sterilized and vaccinated at a centre before being returned to the original site of capture after recovery. In Tanzania, central-point vaccination proved effective for rabies control, as dogs are brought by owners for vaccination (Cleaveland et al., 2003). Similarly, in a programme run by WSPA, the Department of Livestock Development for Zanzibar and local organization ZALWEDA provided sterilization and basic veterinary health care services, initially through a mobile clinic to which dog owners brought their dogs, with additional help from expert dog-handling teams when required. Later in the programme the delivery of these services was increased through local animal health provider clinics. Using capture of roaming dogs for delivery of sterilization when the majority are owned could lead to problems of lack of owner consent, and potentially establishing responsibility for vaccination and sterilization with the intervention staff and not the owners. Similarly, relying on central-point delivery without establishing whether people are willing or able to bring dogs themselves, will lead to low coverage of the dog population.

#### Catch, neuter, and return

Catch, neuter, and return<sup>4</sup> (CNR) essentially involves catching roaming animals, sterilizing them, permanently marking them to show they are sterilized (to avoid recapture), and then returning them to the place from which they were caught, after a period of recovery. Many CNR projects will also vaccinate and treat the animals for parasites at the time of sterilization. The benefits of such an approach can include:

- Reduction in zoonoses transmission.
- Sterilizing roaming animals can improve their health by taking away the energy costs of breeding, and reduces the risks of injury and disease transmission of breeding.
- Sterilizing a roaming animal ensures that it will no longer give birth to offspring that would be likely to suffer and die at a young age.
- Returning a sterilized animal to its original territory reduces migration of other roaming animals into that area; conversely, removing the animal allows migration and increased access to resources which can improve reproductive success of remaining animals.
- Roaming populations can continue to function as biological control of rodents, hence their relatively common use as method of rat population management.

CNR can essentially lead to a stable and healthy population of dogs, if the sterilization rate is maintained at a high enough level. The percentage of dogs that will need to be sterilized will depend upon reproduction rate and survival in the particular population of animals, as described previously. However, CNR alone will not address the roaming dog problem in the long term, while there is an owned population that is not accessible to the catching teams, not being neutered, and potentially providing a source of roaming dogs. Hence CNR alone may not lead to a significant reduction in population size. Instead, it should be seen as a temporary method that stabilizes the current roaming population while additional sources of roaming dogs are also addressed for the long term.

It is also important to be aware that CNR may actually be counterproductive for building a culture of responsible animal ownership, when some of the animals being caught are actually roaming owned dogs, or roaming dogs that the immediate local community considers at least partially their responsibility. In this situation the responsibility for neutering and vaccination should lie with the owners or community. Consequently, a neutering and vaccination programme that is based on community or owner participation and education would be more effective in the long term than CNR.

The following is a list of requirements that must be in place for CNR to be considered as an appropriate method for dog population management. Assessment of the location as described earlier will help to identify if these requirements exist:

- The majority of the population of roaming dogs are unowned. If many of the roaming dogs are in fact community or roaming owned dogs, then the neutering and vaccination programme should be carried out using participation of local people rather than catching dogs on the streets.
- Roaming dogs are a significant source of the next generation of roaming dogs, in other words they are breeding successfully. If dogs on the street do not seem to be able to raise a litter to maturity this indicates that the source of the roaming dogs is owned dogs, and so these should be the target for the neutering programme.
- The environment can support roaming dogs in a good state of welfare. For example, traffic flow is slow or light, and there are reliable food sources available.
- Local people want to maintain the local roaming dog population as part of their community. Without support from local people the programme will not only be difficult to run, but also the safety of the returned dogs will not be guaranteed.
- There is support from both local and national government. Without such support, the safety of returned dogs cannot be guaranteed.
- There is an understanding that CNR will achieve stabilization for the short term and will be replaced in the long term with a programme that will address other sources of roaming dogs and increase responsible ownership, working towards the ultimate goal of all companion animals having responsible and caring owners.

Although CNR can be effective for zoonotic disease control and population reduction (Reece and Chawla, 2006) there are many important limitations on its use. An important principle to consider is that the welfare of every animal that is caught, sterilized, and returned becomes the responsibility of the CNR programme. The return of the sterilized animal to the streets does not signal the end of this responsibility; the likely fate of returned animals must be considered.

The following lists examples of situations where a CNR technique is not suitable. Assessment (as described earlier) will help identify if any of these are relevant for the location in question:

- When the roaming dog population is found to reproduce unsuccessfully (i.e. they are not the source of the next generation of roaming dogs). Sterilization efforts should instead be focused on the true source of roaming dogs.
- Where there is indiscriminate killing of roaming dogs. To return a dog to this situation places its welfare at risk, and to catch and sterilize dogs that will later be killed is a waste of resources.
- Where the environment is unsuitable. Large urban areas with fast-flowing traffic are not suitable for CNR programmes. Releasing a dog into an environment where it is likely to be run down does not constitute good animal welfare.
- Where the local community has intolerance. Not all people like roaming dogs, and there may be strong religious and cultural reasons for negative views towards certain species. Efforts should be made to educate people about the positive consequences of a CNR programme; however, the opinions of local people should be considered, as they have a right to a view on their local environment. It is also very important to consider how local people will react towards roaming dogs once they have been returned. Cruelty and abuse towards roaming dogs is an unfortunate reality that must be considered.

From the above discussion, it is clear that CNR will only be suitable in a restricted

number of situations and may not be suitable across a whole nation or city. This approach may be more suitable for cat population management, as roaming cats tend to match the required criteria more closely than dogs, although this should be tested through an initial assessment.

#### Disease and parasite control

The best form of disease and parasite control in dogs is a programme of regular preventative measures, as opposed to relying solely on surveillance and treatment of cases once they have already occurred. The aim of preventative veterinary measures is to provide animal welfare and human health benefits through reduction in zoonotic diseases. They are sometimes required by law, for example rabies vaccinations in most rabies-endemic countries. These preventative measures usually need regular application, so it is important to consider the sustainability of access to these treatments. Setting up ongoing access through local veterinary infrastructures is usually ideal. If a zoonotic disease transmitted by dogs is identified as the main problem for a particular location, a programme to provide preventative measures on a mass and coordinated short-term scale may be most effective, especially if disease elimination is the goal. For example, the mass annual or bi-annual dog rabies vaccination programmes run in nearly all Latin American countries since the 1980s (Schneider et al., 2005) has led to a significant and widespread reduction in dog and human rabies cases across Latin America.

Combining sterilization with preventative treatments such as rabies vaccination may improve disease control. Although the costs of sterilization are not insignificant (the average full cost of surgical sterilization including medicines, vet time, and infrastructure costs for WSPA-funded projects in 2009 was US\$ 25 per dog, ranging from US\$ 10.30 to US\$ 52 per dog), so an analysis should be completed of whether sterilization costs provide sufficient disease control benefits to warrant the investment. Benefits of dog sterilization to disease control, with rabies control particularly in mind, include the following (WHO and Bill and Melinda Gates Foundation, 2009):

- Sterilization reduces population turnover and so helps maintain herd immunity, especially important if using annual mass vaccination campaigns (see Hampson *et al.*, 2009 for a discussion of the reduction in population level immunity in dog populations with high turnover).
- Offering sterilization and basic treatments can increase owners' compliance, as they gain more benefit for effort of bringing their dogs to an intervention, hence the percentage of vaccinated dogs can increase.
- Sterilization can help to maintain herd immunity by reducing the number of unowned dogs that might be difficult to access for vaccination, by:
- Improving health and reducing problem behaviours of individual dogs, and hence reducing abandonment.
- Reducing the production of unwanted offspring that may otherwise have been abandoned.
- Reducing reproduction of unowned dogs whose offspring are also likely to remain unowned.
- Sterilization also can reduce reproductive behaviours that put dogs at higher risk of contracting rabies. Females in oestrus can cause increased movement of individual animals, leading to increased meeting frequency between dogs and often fighting between males.

# Removing dogs from the street

When initial assessment reveals that a location is not suitable for managing roaming dog populations *in situ*, for example by using CNR, the alternatives are to remove dogs from the public places for euthanasia if they are suffering from untreatable diseases or injuries; reuniting with their owners; rehoming; or euthanasia if rehoming is not possible. Keeping dogs in sanctuaries for life is difficult and expensive to achieve if a reasonable level of animal welfare is to be maintained. While private organizations may achieve this through significant investment of time and funds, such sanctuaries are unlikely to contribute significantly to the wider population management goals and should not be seen as a solution to population management.

Whether run by government authorities, NGOs or private organizations, catching and housing dogs should be subject to agreed standards that ensure an acceptable level of animal welfare is maintained. In some countries the care that should be provided will be defined by the relevant legislation, but inevitably additional protocols will be required to guarantee practices used by all staff ensure the correct care is given. These include, but are not limited to:

- techniques for catching dogs, and their transportation, including limits on number per vehicle;
- initial entrance to the holding centre, including quarantine;
- assessment of dogs prior to rehoming;
- standard veterinary treatment for all dogs including sterilization;
- assessment of the suitability of potential homes and matching dogs;
- clear limits on capacity; and
- a euthanasia policy that has protecting animal welfare as its core principle (see ICAM Coalition,<sup>5</sup> for further discussion of euthanasia, and RSPCA (2006) for further discussion of protocols and management of shelters).

Local authorities may be required by law to provide the capacity to hold dogs for a limited period of time for disease surveillance, for example in the case of a dog that has bitten someone and is suspected to be rabid, or to hold a roaming dog for a minimum period of time to allow the owner to be found (often a 2-week period). Beyond this basic requirement, authorities can provide additional rehoming services, or they may contract out this aspect to non-governmental or private organizations, ideally including a contribution to basic kennelling costs. The cost of running a rehoming centre should not be underestimated, and closing such facilities is extremely difficult. Hence before commitment to such a facility is made, it is advisable to hold sufficient funds for building and running costs for at least 1 year as capital, and to have agreed a clear plan for sustainability. An alternative to rehoming centres is fostering, which may be more cost-effective and better for animal welfare. An example of fostering is given later in this chapter.

When running holding facilities, rehoming centres, or fostering networks, euthanasia will be required for animals that are suffering from an incurable illness, injury, or behavioural problem that prevents them being rehomed, or which are not coping well enough with the facilities to maintain a reasonable level of welfare. Ultimately, a successful population-management programme should create a situation where these are the only occasions when euthanasia is required, and all healthy animals can be found a good home. In reality, however, most countries will not be able to achieve this situation immediately but will need to work towards it, accepting that some healthy animals will be euthanized as not enough homes exist that can provide a good level of welfare. Whenever euthanasia is used, it must employ humane methods that ensure the animal moves into unconsciousness and then death without suffering (ICAM Coalition, 2008; WSPA, 2007).

Removing dogs from public areas may be necessary in many countries where roaming dogs are not tolerated, or when their welfare on the streets is unlikely to be good. In some cases, these dogs are reunited with their owners or rehomed quickly, leading to a positive outcome for animal welfare. However, unfortunately many animals are euthanized after capture due to welfare problems, behaviour problems preventing rehoming, or simply because there are not enough homes. Removing dogs even when the outcome is good should not necessarily be seen as a solution to dog population management problems. Ideally dogs should never become roaming nor unwanted, so removal of dogs must not be relied upon as the sole response, but instead be part of a comprehensive approach to population management which also addresses the source of roaming and unwanted dogs.

# An example of fostering as an alternative to rehoming centres

In an East Asian city with one of the greatest human population densities in the world, a large population of stray dogs, and limited fundraising capacity, many shelters quickly became overwhelmed. In many instances, lack of financial resources and constant demand led to a dramatic fall in standards of care, resulting in significant animal suffering and distress for the staff. As an alternative, a new organization focused on creating a foster network of dedicated volunteers to take abandoned dogs and cats into their homes temporarily.<sup>6</sup>

For its part, the organization agreed to support the animals, paying for all medical bills, vaccinations, and neutering, until long-term homes were found. In the 1st year the organization built up a network of more than 40 foster homes with the goal of reaching 100 within the 2nd year. The animals are rehomed via the internet and the network has the potential to house a far greater number of animals than a shelter ever could. The animals are all homed in appropriate conditions, and the scheme has far lower overheads and administrative costs than a shelter. The new organization has become a success in a city where many similar projects have failed.

## Example: Colombo comprehensive and humane dog population management components

Following on from the assessment and data interpretation completed for Colombo, the following components were selected for the comprehensive, humane, and sustainable programme:

- Mass vaccination of both owned and community dogs across the Colombo Municipal Council area. Rabies outbreak response including vaccination of roaming dogs in an area immediately around any suspected cases.
- Targeted sterilization of both owned and community dogs with a focus on female dogs, and involving maximum community involvement in bringing dogs for sterilization and post-operative

care, using two veterinary mobile clinics. Community dogs are those with no single referral household or person; however, members of the community are recruited by the team to provide post-operative care to the community dogs, encouraging a sense of responsibility over them, as well as ensuring the dogs have oversight during the postoperative period. The efforts to involve the community are aimed at moving dogs along a continuum from unowned to responsible-owned. Making dogs more attractive (e.g. through treatment for skin conditions) and safe (through rabies vaccination) helps to accelerate this process.

- Education of children and adults in bite prevention, rabies awareness, and responsible dog ownership.
- Development of dog managed zones (DMZs). These are areas set up on private premises such as hospitals, schools, and army bases where a population of dogs lives. In collaboration with the owners of these premises the dogs are sterilized and vaccinated; staff and public are educated in their responsibilities and the aims of the DMZ; and good garbage-management practices and feeding stations are set up to reduce potential conflict with people.
- Training of municipal staff in relevant skills including humane dog handling, recognizing dog behavioural signs, delivering responsible ownership messages and bite prevention to communities, and surgical neutering.

#### Summary

There are many components that can be selected and combined to create a comprehensive and humane population management programme. Many involve direct interaction with dogs, and protocols should be developed that ensure practices are humane and also protect the safety of staff. Prior assessment of the location will help determine which components are most suitable, and monitoring and evaluation will provide a measure of what is proving effective and lessons learnt, to ensure the programme continues to evolve and improve over time. This is discussed in the next section.

#### Monitoring and Evaluation

Despite considerable investment in dog population management across the world, investment in monitoring and evaluating its impact is surprisingly low. Monitoring and evaluation should provide significant benefits in the following ways:

- Help to improve performance, by highlighting both problems and successful elements of interventions;
- Provide accountability to those that invest in the programme whether they are authorities or the dog owners themselves, to demonstrate that the programme is achieving its aims; and
- If methods are standardized, compare the success of strategies used in different locations and situations.

Monitoring is a continuous process, usually focused on activities that aim to check programme progress against targets, and allow for regular adjustments. Evaluation is a periodic assessment, usually carried out at particular intervals or 'milestones' to check the programme is having the desired and stated impact. Both monitoring and evaluation involve the measurement of indicators that are chosen because they are quantifiable ways of reflecting the stated objectives of the programme (adapted from OIE, 2009, Chapter 7.7).

Planning of dog population management programmes to include a 'hierarchy of objectives' with indicators of success at each level will support effective monitoring and evaluation. In its simplest form a hierarchy of objectives will include:

 Desired impacts. These are the visible changes that the stakeholders would like to see and may include a reduction in the number of roaming dogs, reduction in dog and human rabies cases, or reduction in number of healthy dogs euthanized in shelters.

- Objectives that, if achieved, will contribute to the desired impacts. These will be the effects of the programme that in combination will help achieve the desired impacts, and may include an increase in sterilization of the dog population (in particular those dogs with low-income owners living in a specified location), increase in rabies vaccination coverage, and improved knowledge, attitudes, and practices relating to dog care and dogbite prevention.
- Activities that will achieve each stated objective. These will be the efforts that the programme makes; what the programme actually does daily to achieve the objectives. These may include:
- a training programme for local vets in low-cost but high-asepsis surgical sterilization;
- provision of a mobile clinic for areas where there is no accessible veterinary service;
- an annual rabies vaccination campaign with a particular focus on low-income areas;
- a school education programme in bite prevention and responsible dog ownership;
- development of improved legislation and enforcement, including regulation of breeding and sale of dogs.

For each level of the hierarchy, indicators are selected that can directly measure any change in the stated objective, and a method of measuring the indicator is similarly stated. For example:

- At the impact level. If the desired impact is a reduction in the roaming dog population, an indicator could be the number of roaming dogs visible on public property between 6 a.m. and 8 a.m. in a selected sample of wards of a municipality. The method of measurement is therefore the direct observation survey, conducted every 6 months.
- At the activity level. If dog reproduction control was selected as an important component of the programme, the number of dogs sterilized through a low-cost sterilization project subsidized

by the programme in collaboration with a local veterinary association would be the indicator. The method of measurement could be the monthly reports submitted by participating veterinary clinics.

From these examples it becomes clear that the indicators to be used for monitoring and evaluation will depend on the objectives selected for the programme, which will reflect the initially identified problems and their causes. However, there are some indicators that are likely to be common to most dog population management programmes, including:

- Indicators of the size of the roaming dog population measured through direct observation surveys of dogs on public property, or the number of dogs collected from public property by authorities. If roaming dog populations are common in the location in question, an additional indicator of the percentage of lactating females measured through direct observation surveys of dogs on public property would reflect the reproductive activity of the roaming dog population.
- Indicators for the size of the unwanted dog population measured through abandonment of dogs at shelters or requested euthanasia at veterinary clinics.
- Indicators for the size of the owned dog population and its overlap with the roaming dog population, measured by asking dog owners about roaming behaviour.
- Combining indicators about the size of the roaming dog population, owned dog population, and where they overlap will lead to indicators for the total dog population size. This can be reported as a total number of dogs for a specifically defined location, a density per unit area, or as a ratio of dogs to humans.
- Indicators of dog welfare measured through direct animal-based measures including body condition score, skin conditions, and incidence of injuries such as those caused by road traffic accidents.
- Indicators of dog care measured through vaccination coverage and percentage of

the population receiving regular internal and external parasite control.

- Indicators for animal cruelty including number of complaints and prosecutions under relevant legislation.
- Indicators for relevant zoonotic diseases such as rabies, measured as the incidence rate per month and per year in both dogs and in humans. This should also include measures of surveillance efforts to ensure changes in incidence reflect actual changes in disease, and not only efforts to record disease incidence.
- Indicators for dog-related injuries to humans measured by monthly or annual rate of dog bites of humans treated by health clinics/hospitals (often reflected by uptake of post-exposure prophylaxis for suspected rabies exposure).

# Example: Colombo monitoring and evaluation efforts

Monitoring and evaluation in Colombo is achieved using a range of methods of measurement, including:

- Direct observation and counts of roaming dogs in the early morning (peak time for roaming dogs) including scoring individual dogs for body condition, skin condition, and lactation in the case of females.
- Questionnaire survey of both dog owners and people who do not own dogs.
- Evaluation immediately following education programmes to assess comprehension and follow-up 6 months later in a sample of classrooms, to assess knowledge retention.
- Official data sources, including dog and human rabies cases, and reported dog bites from local and central government.
- Qualitative measures such as collating testimonials from expert witnesses, and 'most significant change' stories (a method of collecting qualitative information in the form of stories of change experienced by beneficiaries; see Davies and Dart (2005) for more information).

## Summary

Although time consuming and not without financial costs, monitoring and evaluation of dog population-management programmes should quickly provide benefits that outweigh these costs in terms of learning to improve programme performance. They should also provide a level of accountability that is demanded of both public funds and private donations to NGOs. The indicators selected for each programme should reflect the objectives selected by that programme to match the problems and causes initially identified, although some common indicators are suggested in this section to inspire programme managers to start monitoring and evaluating interesting indicators of success.

#### Final example: Colombo achievements

Throughout this chapter a particular programme was used to provide a working example as an illustration. To complete this, the achievements of this programme from mid-2007 through to mid-2010 are summarized:

- The project has set out to provide an effective and humane alternative to the previous approach of regular dog impounding and elimination using inhumane methods, including gassing with exhaust fumes. This alternative project including vaccination, sterilization, and education has been well received and accepted by the municipality and the local communities, and is set to be maintained by local government from 2012 onwards. The impacts on human health and animal welfare have been positive, most notably with a decline in dog rabies cases from 2008 onwards to well below previous annual fluctuations (Fig. 11.2).
- The percentage of lactating female dogs seen on the streets during direct observation surveys has fallen from a mean of 8% (maximum observed 21%) in June 2007 to 1.1% in June 2010 (maximum observed 5%). This reduction suggests that reproduction in the roaming dog population has diminished.



Fig. 11.2. Dog rabies cases in Colombo Municipal Council set against elimination, vaccination, and sterilization from 1990 to June 2010. BPT, Blue Paw Trust.

The percentage of lactating roaming female dogs is significantly and negatively correlated to the percentage of sterilized females seen on the streets (R2 = 0.33, df = 59, p<0.001), suggesting every 1% increase in the population sterilized leads to a decrease of 0.1% in the percentage of lactating females.

- At the same time the body condition and skin condition of the roaming dog population have improved; not only in sterilized dogs (as expected due to eliminating the energetic demands of breeding), but also in unsterilized dogs, suggesting there has been some improvement in the care provided by the community to both sterilized and unsterilized dogs.
- The roaming dog population size has shown a slight increase over time, but there is some evidence that the rate of increase has slowed and then started to decrease in recent months. Whether this decrease continues will be closely monitored in coming months and years. The initial increase in population size may be due to the project starting 1 year after elimination of dogs had been stopped, when the dog population was presumably recovering, having been kept below the carrying capacity of the environment through consistent removal by elimination.
- The education programme on bite prevention and rabies awareness has

shown both an increase in knowledge immediately following lessons and also an impressive level of retention over time. Using a standard set of questions, it was found that 86% of primary school children and 90% of secondary school children had gained the required knowledge immediately after the education session and that retention was good, with 85% of primary and 78% of secondary school children having maintained this same level of knowledge after 6 months. This will need to be further evaluated with data on dog bites for children in the CMC as compared to dog bites in the rest of the country.

The main challenges remaining will be to ensure a suitable national and local legislative foundation for this project and others like it, and to establish the source of future sustainability once WSPA funding comes to an end. However this is already a project for Colombo to be proud of, and in response WSPA is beginning to invest in helping the replication of the approach used to develop this programme in other locations, in particular in South and South-East Asia. However, this programme also has relevance in other locations within Sri Lanka and the project partners hope to support shared learning wherever individuals, organizations and authorities with similar aims are found.

## Conclusion

Dogs fulfil many roles in society and so provide many benefits to humans. However, they can also cause difficulties and experience welfare problems themselves. The aim of dog population management is to utilize a comprehensive set of components or activities to manage populations humanely, so maximizing the benefits of dogs while minimizing the problems they can present. Using a process of initial assessment and data interpretation that relate to the dog population, and human attitudes and behaviours towards dogs, can help with the design of population management programmes suitable for specific locations and so maximized for efficiency and effectiveness. Continuous monitoring and regular evaluation can also help to assess whether programmes are going to plan and are as efficient and welltargeted as possible.

Finally, it is the responsibility of population management programme designers and implementers to ensure that the programme is humane and minimizes any potential animal suffering. The decision to own or care for a dog is rarely a purely functional choice, and usually entails an emotional component. Hence dog owners and carers will expect that management programmes respect this bond between dogs and humans. It is also our moral obligation to manage humanely a situation that arguably humans have created through the domestication of dogs for human benefit.

#### Notes

<sup>1</sup> The International Companion Animal Management (ICAM) Coalition is a coalition of non-governmental organizations with experience of dog population management in a range of countries.

<sup>2</sup> www.icam-coalition.org/resources.html, accessed 17 July 2012.

<sup>3</sup> www.biosecurity.govt.nz/animal-welfare/codes/dogs, accessed 19 June 2012.

<sup>4</sup> This section is amended from chapter 1 of WSPA's Member Society manual. CNR is given many names, including trap, neuter, and return (the term usually used for cat population management) and animal birth control. Although the latter is a general term for reproduction control, in India this term is included in national legislation as a definition of CNR and the method of dog population management for the whole country; hence the common use of ABC as an alternative term for CNR.

<sup>5</sup> Document is available as a download from www.icam-coalition.org, accessed 17 July 2012.

<sup>6</sup> Adapted from RSPCA, 2006.

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# **12** Zoonoses Prevention, Control, and Elimination in Dogs

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A small number of diseases transmitted from dogs to humans have been recognized as representing a significant public health risk requiring the initiation of usually governmentsponsored large-scale prevention and control activities. Two parasitic diseases, namely cystic echinococcosis (Echinococcus granulosus) and visceral leishmaniasis (Leishmania infantum), and rabies, a viral disease, fall into this category. Although these diseases are present in both the developed and developing world, their public health burden mostly falls on poor populations living in developing countries. These zoonoses belong to the group of 'neglected zoonotic diseases', meaning that their public health significance is not well recognized and their control not well addressed by national and international authorities. For all these reasons, these zoonotic diseases are included in the first WHO (World Health Organization) report on 'Working to overcome the global impact of neglected tropical diseases' launched by the Director-General of WHO on 14 October 2010. Their epidemiological cycles and pathways for human infection differ, as well as the tools available to tackle them. Prevention and control interventions in humans and animals are therefore disease-specific, with

the exception that in all three diseases dogs are involved as the main source or reservoir of the causal agents. Consequently, the first measures at hand to combat these diseases aim at controlling the infectious agent at source. Dog population control activities have since been complemented by more direct methods for disease control based on diagnosis and treatment (echinococcosis and leishmaniasis) and disease prevention by dog immunization (rabies). In addition, data acquired on dog populations and their characteristics, particularly in developing countries; experience accumulated in largescale dog reproduction control; and new dog population management guidelines recently produced by international governmental and non-governmental organizations stressing the importance of ethical and animal welfare considerations, are all beginning to have a marked influence on control strategies applied to combat these three diseases in affected countries.

This chapter reviews the past and current situation regarding prevention and control strategies for these diseases and tries to identify, on the basis of existing research, future trends for their control and the feasibility of their elimination.

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## **Dog Rabies Control**

Rabies is found in all continents across the globe, with only Japan, New Zealand, and smaller island nations of the Pacific Ocean considered rabies-free. A range of species is involved in maintaining rabies virus variants (Rupprecht et al., 2008). Bats harbour rabies or rabies-related viruses in most continents. Rabies cases in North America are dominated by raccoons, skunks, coyotes, and foxes (Rupprecht et al., 2002). In much of eastern Europe, the Russian Federation, and Siberia, foxes and raccoon dogs are reported hosts (Matouch, 2007; Wandeler, 2007); while wolves, jackals, and foxes have been implicated in the Middle East (Seimenis, 2007). Wildlife rabies occurs in few Asian countries, except the Republic of Korea where it circulates in raccoon dogs (Kim et al., 2005, 2006). In most of Africa, rabies is maintained in domestic dog populations only (Rhodes et al., 1998; Bingham, 2005; Lembo et al., 2008), but in the southern-eastern part of the continent jackal and mongoose rabies also circulate (Bingham, 2005; Nel et al., 2005). Infected wildlife including bats can transmit rabies to humans, but the total number of cases is very limited. The only exception is widespread vampire bat rabies in Latin America, where clusters of human deaths associated with bat contact have been reported in the Amazon forest, particularly in Brazil and Peru (Salmon-Mulanovich et al., 2009; Castilho et al., 2010).

Despite this variety of wildlife involved in rabies maintenance, the vast majority (>99%) of human rabies cases throughout the world are transmitted by dogs (Knobel et al., 2005). Dog rabies is endemic in most developing countries (WHO, 2010a), with the greatest burden in Africa and Asia, where an estimated 55,000 people die from dog-mediated rabies annually (Knobel et al., 2005; WHO, 2005). In the Eastern Mediterranean region and in a few countries in Latin America, rabies in dogs has mostly been controlled, but still circulates in a few endemic foci (Schneider et al., 2007). This section provides an overview of the current and historical situation of dog rabies and dog rabies control, before discussing strategies for dog rabies elimination.

### Historical perspectives and current trends

In many parts of the world rabies control has been spectacularly successful, with entire continents achieving canine rabies elimination. Yet, elsewhere, dog rabies remains a problem, and in some locations where elimination had previously been achieved re-emergences have since occurred. In the next section we overview the approaches historically used to control rabies, and provide examples of countries that have successfully controlled or eliminated canine rabies, as well as how these successes were achieved.

#### Pre-vaccination era

The similarity between animal and human rabies and the distinctive transmission pathway through the bite of an infected animal meant that rabies was identified earlier than most other zoonoses. However, there was no efficacious human prophylaxis after exposure to a rabid animal before Pasteur's vaccine was applied for the first time in 1885. As a consequence, measures for controlling rabies historically targeted the domestic dog, the species mostly involved in transmission to humans. Before the advent of the first veterinary vaccines against rabies during the 20th century, measures for dog rabies control consisted of movement/contact tracing and restriction (confinement, leashing, muzzling) of rabid animals and their contacts, notification of cases, and culling of rabid, bitten and 'stray' dogs the so-called 'classical' methods (Bögel, 2002). Measures such as compulsory muzzling, dog movement control, and destruction of strays, respectively, were recommended as early as the 6th century BC by the Avesta in India and in the 4th century AD by the Talmud, as well as in China in the 2nd century BC and in ancient Greece and the Roman Empire (Blancou and Meslin, 2000). However, it took until the 18th century for such measures to become widespread in Europe, with dog muzzling becoming compulsory only at the end of the 19th century in the United Kingdom and France (Blancou and Meslin, 2000).

During the 19th and first half of the 20th century, classical control methods led to the elimination of rabies in dogs in some areas of Europe (see Table 12.1 for examples). Removal of strays and strict enforcement of a sanitary policy brought rabies under control in Scandinavian countries in the 19th century (Tierkel, 1959; WHO, 1987). Enforcement of legislation, including dog muzzling, tracing and restrictions of dog movements, destruction of strays and a strict import regulation policy eliminated canine rabies from the UK in 1902 and again in 1922, after its reintroduction in 1918 during World War I (Fooks et al., 2004; Meldrum, 1988; Muir and Roome, 2005).

## Post-vaccination era

Mass vaccination of dogs started in Japan in 1921 (Umeno and Doi, 1921) and was very successful in controlling rabies until the disease was reintroduced during World War II (Shimada, 1971). After the war, vaccination efforts were renewed and since 1957 Japan has been free of rabies, except for three imported cases of human rabies (from Nepal and the Philippines) in 1970 and 2006 (Shimada, 1971; Takahashi-Omoe et al., 2008). Together with its geographical isolation, the establishment of a countrylevel rabies management system focusing on compulsory registration and vaccination of domestic dogs, regulations for import and export of animals, and continuous upgrading of countermeasures against rabies have kept the country rabies-free (Takahashi-Omoe et al., 2008). In the late 1930s, mass vaccination was introduced in Hungary, where the first field trials demonstrating the feasibility of dog rabies elimination through a combination of vaccination and classical measures were conducted (Lontai, 2004; Manninger, 1968). Following this model, dog vaccination was included in national rabies management programmes in numerous European countries, with canine rabies being eliminated from large areas of Western Europe throughout the 20th century (see Table 12.1 for examples).

Japan is not the only Asian country to have achieved rabies elimination in the 20th century. Compulsory mass vaccination, stringent legislation, and intensive destruction of strays eliminated rabies from Malaysia in 1953 (Wells, 1954), with only periodic reintroductions from the Malaysia-Thailand border, probably due to relaxation of rabies control measures across the cordon sanitaire (Tan et al., 1972; WHO, 1988). In 1996, one isolated, probably imported, dog rabies case was reported outside the buffer zone (Hussin, 1997), but no cases in Malaysia have been reported since. National programmes to control rabies in Korea, including mass dog vaccination, also led to dramatic declines and rabies elimination from 1945 until 1992 (Kim et al., 2006). Subsequent re-emergence of rabies from the areas bordering the demilitarized zone in 1993, and persistence ever since, has been attributed to the involvement of wildlife hosts (Kim et al., 2005).

During periods of colonial occupation in Africa, rabies was successfully controlled in some countries, through mass vaccinations combined with strict implementation of tie-up orders and shooting of roaming dogs (Shone, 1962). But these control measures deteriorated over the second half of the 20th century, while human and dog populations have grown exponentially, making dog rabies control increasingly difficult. The result has been that dog rabies has since increased unabated throughout most of sub-Saharan Africa and Asia (Knobel *et al.*, 2005).

Domestic dog rabies has been largely controlled in North America since the 1960s through mass vaccination campaigns followed by a long period of compulsory pet vaccination (Blanton et al., 2007; Held et al., 1967; Korns and Zeissig, 1948). However, the United States was only declared free of dog rabies in 2007 (Blanton et al., 2007) after concerted transboundary collaborations to prevent importations. In Latin American countries, national programmes for the control of dog rabies, initiated in 1983 based mainly on mass immunization of dogs, interrupted dog-to-dog rabies transmission and eliminated human rabies from most urban areas in that part of the world (Schneider et al., 2007, 2011).

## Table 12.1. Examples of successful control or elimination of canine rabies.<sup>a</sup>

Continent	Country	Methods of control	Elimination Y/N	Year achieved	References
Africa	Zimbabwe	Pre-vaccination era: muzzling (later abandoned); registration, dog confinement, destruction of strays and Dog Tax Ordinance	Y	1914 (until 1938)	(Shone, 1962)
	Zimbabwe	Post-vaccination era: compulsory dog vaccination (mainly), tie-up orders, and destruction of unowned dogs (secondary measures)	N (dramatic declines except eastern and western border areas with Mozambique and Botswana. Due to unrest and civil war, re-establishment since 1965 up until now)	1961	(Shone, 1962)
	Tunisia	National programme including dog vaccination and removal of unvaccinated dogs	N (dramatic declines)	1986	(Chadli <i>et al.</i> , 1976; Osman and Haddad, 1988; Matter <i>et al.</i> , 2004)
	Western Zambia	Mass destruction of tribal dogs	Y (in one large tribal area, but re-establishment since 1913 onwards)	1901	(Edmonds, 1922; Snyman, 1940)
	KwaZulu-Natal	Dog vaccination and population control	N (temporary control)	1960s	(Mansfelt, 1962; Swanepoel <i>et al.</i> , 1993)
Americas	USA	Widespread vaccination; pet care; stray dog control (in 1960s)	Y (except for a few border areas)	1940–65	(Johnson, 1948; Korns and Zeissig, 1948; Tierkel, 1959; Humphrey, 1966; Held <i>et al.</i> , 1967; Blanton <i>et al.</i> , 2007)
	USA	Measures continued as above, with education, as well as oral vaccina- tion to eliminate the dog-coyote rabies virus variant in Texas	Y	2004	(Held <i>et al.</i> , 1967; Kelly, 1980; Blanton <i>et al.</i> , 2007; Velasco-Villa <i>et al.</i> , 2008)
	Central America (Belize, Honduras, Nicaragua, Panama and Costa Rica); Southern American cone (Chile, Argentina, Uruguay, Paraguay); Guyana, Suriname, French Guiana, most of Caribbear (except Cuba and Haiti)	Mass vaccination; decentralization and timely provision of PEP; national and international multi- sectoral cooperation; dog popula- tion control; epidemiological surveillance; and education	N (but no human rabies transmitted by dogs for 3 years despite canine rabies still circulating )	2004	(Schneider <i>et al.</i> , 1996, 2005, 2011)

	Brazil, Peru, Colombia, Venezuela Mexico, Guatemala, Cuba	<ul> <li>Mass vaccination; decentralization and timely provision of PEP; national &amp; international multi- sectoral cooperation; dog population control; epidemiological surveil- lance; and education</li> </ul>	N (but no human rabies transmitted by dogs at sub-national level for 3 years; active circulation in localized foci)	2004	(Chomel <i>et al.</i> , 1987; Belotto, 1988; Larghi <i>et al.</i> , 1988; Schneider <i>et al.</i> , 1996, 2005, 2011; Belotto <i>et al.</i> , 2005)
Asia	Japan	Mass vaccination	Y until reintroduction during World War II	1930	(Shimada, 1971)
	Japan	Compulsory mass vaccination; strict importation rules and movement restriction	Y	1956	(Shimada, 1971)
	Singapore	Stray dog elimination, enforcement of sanitary policy	Y	1892	(West, 1972)
	Malaysia	Licensing and compulsory mass vaccination; destruction of unowned/ unvaccinated dogs; development of an immune belt to prevent entry of rabies from Thailand	Y until reintroduction during civil unrest in 1970. Sporadic cases near Thai border since	1956	(Wells, 1954, 1957; Tan and Shukor, 1985)
	Hong Kong	Quarantine/observation of imported dogs/cats and biting animals; dog licensing/vaccination; stray dog control; and laboratory based surveillance	Y (but imported in 1980)	1956	(Cumming and Rex, 1952; Cheuk, 1969)
	Philippines (central)	Laboratory-based surveillance, community education, mass vaccination	Success in vaccinated areas. Re-emergence when coverage dropped, now endemic through most of country	1964–72	(Beran and de Mira, 1966; Beran, 1971; Beran <i>et al.</i> , 1972)
	Taiwan	Mass vaccination	Y	1961	(WHO, 1987)
	Republic of Korea	Mass vaccination, mostly of dogs	Y (Raccoon dog rabies emerged in 1993	1985	(Hyun, 2005; Kim <i>et al.</i> , 2006)
	Maldives, Lakshwadeep, Andaman, and Nicobar islands	Traditionally rabies free. Import of dogs prohibited by law in Maldives to maintain freedom from rabies	Rabies-free		(WHO, 1998b)

Continued

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## Table 12.1. Continued.

Continent	Country	Methods of control	Elimination Y/N	Year achieved	References	
Eurasia	Scandinavia	Stray dog elimination, enforcement of sanitary policy	Y	pre-1900	(Tierkel, 1959)	
	The Netherlands	National legislation to control rabies in dogs and cats	Y	1923	(Aubert <i>et al.</i> , 2004)	
	Prussia	Stray dog elimination, enforcement of sanitary policy	Initial success but subsequent introductions in 20th century	1875	(West, 1972)	
	Germany	Destruction of stray/rabid/suspect dogs, enforcement of sanitary policy, quarantine of dogs,	Y (except for border areas with Lithuania, Poland, France, and Czech Republic)	1914	(Müller and Müller, 2004)	
		notification of rabies dog muzzling [Reichsviehseuchengesetz (Imperial Animal Disease Act) 23 June 1880	Y (territory comprising Germany as it exist today until outbreak following World War II)	1939	(Müller and Müller, 2004)	
	Austria	Stray dog elimination, enforcement of sanitary policy	Y	1914	(Müller and Müller, 2004)	
	Denmark	Stray dog elimination, enforcement of sanitary policy	Y	1889	(Müller, 1971)	
	UK	Destruction of stray/rabid dogs; dog muzzling; movement restriction; tracing movements of rabid dogs and their contacts	Y (until outbreak following World War I)	1886–1903	(Meldrum, 1988; Fooks <i>et al.</i> , 2004; Muir and Roome, 2005)	
		Destruction of stray/rabid dogs; dog muzzling; movement restriction; tracing movements of rabid dogs and their contacts; and strict import regulation policy	Y	1922	(Meldrum, 1988; Fooks <i>et al.</i> , 2004; Muir and Roome, 2005)	
	Czechoslovakia	Mass vaccination	Y	1921–1939	(Matouch, 2004)	
	France	Dog registration; vaccination; and destruction of strays	Y	1960	(Aubert <i>et al</i> ., 2004)	
	Spain and Portugal	Pre-vaccination era: destruction of suspect rabid and contact animals; compulsory muzzling; killing of strays; and habitat control	Y (except dog rabies imported outbreak in Malaga, 1975)	1960 (Portugal), 1966 (Spain)	(Abellan Garcia <i>et al.,</i> 2004)	

		Post-vaccination era: compulsory dog registration and vaccination; and impounding and destruction of unclaimed dogs	Y	1975–1978	(Diaz Yubero <i>et al.</i> , 1982; Abellan Garcia <i>et al.</i> , 2004)
	Greece	Compulsory collaring of owned dogs and destruction of uncollared dogs; establishment of PEP stations; and compulsory dog vaccination	Y	1987	(Mutinelli <i>et al.</i> , 2004)
	Italy	Strict dog registration, ownership tax collection, seizure of strays and segregation of biting dogs and (since 1950) compulsory vaccination	Y (except imported cases from bordering countries)	1973	(Mutinelli <i>et al.</i> , 2004)
	Yugoslavia	Mass vaccination	Y	1946–91	(Mutinelli <i>et al</i> ., 2004)
	Hungary	Mass vaccination; movement and contact control; and stray dog control	Y	1935–44	(Manninger, 1966; Lontai, 2004)
	Finland	Vaccination and dog control	Y	1930s; 1960s	(Westerling et al., 2004)
	Israel	Compulsory dog vaccination and stray elimination	N (Initial success, but subsequent return after end of field trials)	1951	(Kaplan <i>et al.</i> , 1954; Osman and Haddad, 1988; Yakobson <i>et al.</i> , 2004)
Oceania	Guam	Compulsory leashing/confinement and vaccination of pet dogs, destruction of stray dogs/cats, education of the public, embargo upon importation/quarantine of dogs and cats, establishment of surveillance measures and provision of human biologicals	Y	1967	(Glosser and Yarnell, 1970)

<sup>a</sup>PEP, Post-exposure prophylaxis.

### The 21st century

The Americas have been the greatest rabies control success story of the 21st century. Since the city-based mass vaccination programmes that began in the 1980s, efforts have been rolled out into rural areas with approximately 45 million dogs vaccinated a year, and, by 2003, the number of cases of dog-transmitted human rabies in the region had fallen by >90% (Schneider et al., 2007). Since then, <50 human rabies deaths have been reported annually in the Region of the Americas (with the exception of Haiti), the majority still resulting from contact with dogs. Dog rabies is, however, still widespread in Cuba, the Dominican Republic, El Salvador, Guatemala, Haiti, and the Plurinational State of Bolivia (WHO, 2010b; Schneider et al., 2011). In 2008, the 15th Inter-American inter-ministerial meeting on health and agriculture set a target for eliminating dog rabies in Latin America by 2012 (WHO/PAHO, 2008), which after review by the Regional Committee was moved to 2015 (WHO/PAHO, 2009).

Endemic dog rabies has been eliminated from the European Union through a combination of mass vaccination and 'classical' measures, as described above (see also Table 12.1). However, occasional introductions, particularly from North Africa, have had significant economic ramifications (Lardon et al., 2010). In contrast, dog rabies still exists as a problem in Eastern Europe, although the number of human rabies deaths is limited (Bourhy et al., 2005). Russia alone reports from 10 to 20 human rabies deaths every year and high numbers of cases in pets (more than 1500 in 2008, representing >34% of all animal rabies cases), particularly dogs (S. Rybakov, 2009, pers. comm.). Georgia and Ukraine reported an average of 9 and 3 human rabies deaths per year, respectively, during the period 2000-2009 (Aylan et al., 2011). A total of 29 deaths occurred in Turkey from 1999 to 2009 (Aylan et al., 2011), and a nationwide fox and dog rabies elimination programme was launched in 2005 with support from the European Union. The rabies situation in several countries such as Azerbaijan, Tajikistan, and Uzbekistan is also not well known (Gruzdev, 2008). Albania, the former Yugoslav

Republic of Macedonia, and Greece reported the absence of rabies to WHO in 2008 (Aylan *et al.*, 2011).

Although dog rabies is present in all countries of the South-East Asian region, several countries have also recorded successes and a number of countries are committed to eliminating human and dog rabies by 2020 (ASEAN, 2008). In Thailand, Sri Lanka, Vietnam, and Nepal national plans for control and elimination of dog rabies have been developed. Progress is evident in Thailand where eight human rabies cases were reported to WHO in 2008 compared with 74 in 1995 (RIA, 2009). Similarly, Sri Lanka reported 55 cases compared with the >100 cases occurring annually in previous years, and large reductions in human rabies were seen also in Vietnam between 1994 and 2008. although in 2007 clusters of human cases still occurred in 25 out of 63 provinces in both the North and South of the country (RIA, 2009). Nepal has also made significant progress in prevention and control of rabies, and now produces its own human and veterinary rabies vaccines. While Sri Lanka has implemented a programme that has resulted in progressive increases in vaccination coverage in domestic dogs over the last three decades (Kumarapeli and Awerbuch-Friedlander, 2009), the reductions of rabies cases in Thailand and Vietnam have been largely due to improved availability and accessibility of rabies post-exposure prophylaxis (PEP). However, these PEP interventions have also been costly since there have not been concomitant improvements in dog rabies control, surveillance, or PEP prescription based on the status of the biting animal, and therefore PEP rates remain very high. Rabies is still widely distributed in the Philippines, where around 250 rabies deaths are reported annually (RIA, 2009). In this country a special programme aims at eliminating rabies from the entire archipelago of the 'Visayas' by the end of 2013 and obtaining rabies-free status by 2015 (WHO, 2007a). The Visayas comprise a number of islands located at the centre of the archipelago with a population of about 18 million people and an estimated 2 million dogs. A number of smaller islands in the Visayas have been declared rabies free,

for example Apo and Siquijor islands, or are targeted for rabies freedom before 2015, such as Bohol (ARC, 2008).

The rabies epidemiological situation has been worsening over the past 15 years in Indonesia with spread eastwards since the late 1990s and emergence on historically rabies-free islands, such as Flores in 1997 (Bingham, 2001; Windiyaningsih et al., 2004), Maluku and Ambon in 2003, Bali in 2008, and Nias islands in 2010 (G. Tallis, Jakarta, 2010, pers. comm.). The rabies epidemic on Flores island which started at the end of 1997 resulted in a least 113 deaths during the period 1998-2002 (Windiyaningsih et al., 2004) and is still entrenched in 2010. The island of Bali was free of rabies until its confirmation in late 2008. Although mass vaccination campaigns were conducted in villages around the index case, rabies spread to all provinces on the island and by February 2011 more than 100 human deaths had occurred (CDC, 2011). Dog rabies control activities that were carried out by the provincial veterinary services prioritized indiscriminate dog culling operations rather than dog vaccination campaigns, but were ineffective in preventing rabies spread. However, in late 2010 the Bali provincial authorities committed to an island-wide mass vaccination campaign to inoculate nearly 400,000 dogs against rabies, aiming to make Bali rabies-free in 2012 with the technical and financial support of the World Society for the Protection of Animals (WSPA) and direct involvement in field operations of a local organization named Bali animal welfare association (Bawa).<sup>1</sup>

Dog rabies is estimated to kill about 20,000 people annually in India (Sudarshan *et al.*, 2007). However, following the initiation of a number of dog rabies control programmes in major cities (e.g. Bangalore, Chennai, New Delhi, Mumbai, Jaipur) (Reece, 2007) based on dog capture, vaccination, and release, as well as the wider availability of mostly locally produced cell-culture rabies vaccines and immunoglobulin for PEP, the number of human rabies deaths is thought to have decreased considerably during the second half of this decade (M.K. Sudarshan, Bangalore, 2010, pers. comm.).

Rabies is a re-emerging public health risk in China. Dog rabies killed between 4000 and 7000 people a year during the period 1979-1989, but was very swiftly brought under control in 5 years with only 159 human rabies deaths reported in 1996 (Tang et al., 2005). Yet the disease re-emerged progressively, to reach 3300 notified human rabies deaths in 2007, mostly from six south-central provinces (Fu, 2007). Disease re-emergence was associated with a lack of government commitment, relaxation of control measures, including dog vaccination, and ineffective local animal vaccines (Hu et al., 2008), coupled with increasing populations and poor awareness (Wu et al., 2009). Initially, authorities resorted to mass culling as a major tool for dog rabies control (BBC, 2006; CBC, 2009). Following public education campaigns and control activities conducted in the most affected provinces the number of notified human rabies deaths decreased to 2215 in 2009, but around 8 million PEP regimens are administered annually nationwide, and this number is continuously increasing (Q. Tang, Beijing, 2010, pers. comm.).

Most African countries report the presence of human and dog rabies in all or large parts of their territories. In most countries, dog vaccination coverage remains far below the required threshold of 70% (Lembo *et al.*, 2010), and the accessibility and affordability of human vaccine is still very limited, especially to the populations most at risk (Hampson *et al.*, 2008). Since early 2009, South Africa and the United Republic of Tanzania have begun projects working to eliminate human and dog rabies from pilot areas within 5 years (WHO, 2007a).

### Strategies for dog rabies control and elimination

Approaches to rabies control and prevention include strategies directed at humans (pre-exposure or post-exposure prophylaxis) and measures targeting the species mostly responsible for transmission to humans. While both approaches are ultimately aimed at protecting human health, for infection to be eliminated control measures must be directed at the species involved in rabies maintenance in any given area. Here we focus on veterinary measures adopted for the control and eventual elimination of dog rabies in a range of settings.

Since the development of effective animal vaccines for rabies, mass vaccination has become an integral component of rabies control measures. However, the elimination of rabies requires several additional components to mass vaccination, including effective engagement of communities and policymakers, dog population assessment and management, and surveillance capacity and legislation. High levels of awareness amongst key players in rabies prevention and control is vital for effective policy towards canine rabies elimination, including allocation of resources, defining specific roles among all sectors responsible for rabies control and establishing legislative frameworks (e.g. compulsory dog registration and vaccination, animal movement control, and habitat management). Education and promotion of responsible dog ownership should also be considered critical to enhance the effectiveness of dog population management and vaccination efforts.

#### Surveillance

Surveillance is an essential part of rabies control efforts, and is necessary to determine the rabies situation at the start of a control programme and monitor progress towards elimination. Surveillance becomes increasingly important for the demonstration and maintenance of freedom from disease, as has been demonstrated in the Americas.

Most surveillance relies on laboratory confirmation and therefore requires a system for the collection and submission of samples as well as local capacity for performing standard diagnostic tests (the direct fluorescent antibody test, DFA) (Meslin and Kaplan, 1999). In many parts of the world though, particularly in Africa, facilities for fluorescent microscopy are not available, or equipment is not adequately maintained, and capacity for sample collection in the field is limited. Hence, reported laboratory-confirmed cases are lacking and may not necessarily provide a good measure of the incidence of rabies in an area. Alternative tests for rabies are now available which show promising results, require simpler infrastructure, and are less expensive. Specifically, the direct rapid immunohistochemical test (DRIT) has been validated on field diagnostic material from developing countries and has shown complete concordance with the gold standard DFA (Lembo *et al.*, 2006; Durr *et al.*, 2008; Tao *et al.*, 2008) and lateral-flow immunodiagnostic test kits are proving useful surveillance tools (Kang *et al.*, 2007; Markotter *et al.*, 2009).

Reporting of suspect cases and hospital records of animal-bite injuries from suspect rabid animals can be very useful because of the characteristic clinical signs of rabies that are accurately recognized by local communities (Hampson et al., 2008; Lembo et al., 2008; Beyer et al., 2011). Hospital records also contain information on numbers of PEP regimens delivered, which can provide some indication of rabies trends, but may also reflect inadequate health service provision. In many developing countries, data collected at the national level are often based on clinical signs rather than laboratory diagnosis, and are largely incomplete (Dodet et al., 2008). Channels of reporting and communication, including the submission of samples for laboratory diagnosis, therefore need to be improved, as officially reported records currently underestimate the true incidence of rabies.

#### Dog vaccination

Vaccination of 70% of the dog population has repeatedly been shown to be effective in eliminating endemic canine rabies (Coleman and Dye, 1996). Although lower levels of coverage can sometimes be effective, in many developing countries mortality and birth rates in dog populations are generally high and therefore campaigns need to be repeated to prevent coveragefalling to ineffective levels (Hampson *et al.*, 2009). High vaccination coverage (70% or higher) can be attained through strategies consisting of well-designed educational campaigns, intersectoral cooperation, community participation, local commitment in planning and execution, availability of recognized quality vaccine, media support, and effective general coordination and supervision of the activities (Schneider *et al.*, 2007). However, a variety of operational approaches for mass dog vaccination is available, differing in suitability and effectiveness depending upon the setting.

In most settings domestic dogs have been found to be highly accessible for parenteral vaccination, even when the majority of dogs appear unrestrained and no owners are evident (Perry, 1993; Wandeler et al., 1993; Robinson et al., 1996; Kayali et al., 2003; Kongkaew et al., 2004; Suzuki et al., 2008; Ratsitorahina et al., 2009; Lembo et al., 2010). Three basic approaches to mass vaccination campaigns have been adopted, either alone or in combination, to control rabies in canine rabiesendemic areas: (i) house-to-house visits; (ii) continual vaccination at fixed vaccination posts in well-recognized sites within the community (including private or government veterinary clinics); and (iii) mobile teams which set up temporary vaccination posts (central point vaccinations). The choice of approach will depend on the specific community, and the decision should be taken at the local level.

In terms of the costs and logistics, central point vaccinations are generally the most efficient (Kaare et al., 2009). In Latin America, pulsed mass vaccinations at central points have been conducted free of charge on an annual basis with high coverage (around 80%) achieved in a short period of time (no more than 1 week) (Belotto, 1988, 2001; Schneider et al., 2007; Lucas et al., 2008). Charging for vaccination is usually counterproductive, as turnout may be too low to achieve adequate vaccination coverage. In Chad, owners were found to be only ready to pay an amount (USD 0.78-1.36 per dog) that was substantially less than the total cost of having a dog vaccinated (Durr et al., 2009). A potential alternative to charging is to encourage voluntary contributions, avoiding a perception of coercion. However, rabies control is a public good and if a threshold vaccination coverage of ~70% cannot be reached, dog rabies is unlikely to be controlled, resources will be wasted, and communities and field veterinary staff demotivated.

To achieve coverage of 70%, governments should therefore be ready to substantially subsidize dog vaccination campaigns.

In some circumstances (e.g. for very aggressive or truly unowned dogs, and in dispersed communities) alternative delivery strategies may be required to achieve high levels of vaccination coverage. Oral vaccination of dogs has been shown in various settings to lead to significant increases in coverage (especially of ownerless and poorly supervised owned dogs), both when applied exclusively or in combination with parenteral vaccination (Matter et al., 1995, 1998; Guzel et al., 1998; WHO, 2007b). Yet, more than 10 years after the WHO Oral Vaccination Delivery (OVD) Group had its last meeting (WHO, 1998a), OVD has neither become the 'key to dog rabies elimination', as it was expected (Meslin et al., 2000), nor a convincing operationalized component of any dog rabies control and elimination programme. The major obstacle in some countries is concern over safety of the rabies or vector virus strains for humans, whereas in others it is mostly an economical issue, as cost per currently available commercial vaccine bait is manyfold greater than the cost of an injectable vaccine. Baits produced locally (Estrada et al., 2001), incorporating a vaccine strain known to be safe and efficacious (WHO, 2007b), could however make oral vaccination more affordable.

To determine the effectiveness of vaccination efforts and whether sufficient numbers of dogs have been reached or supplementary follow-up measures are necessary, vaccination coverage needs to be measured. This also requires an initial determination of the dog population size and growth rates. Registration and permanent identification of vaccinated dogs is recommended. However, lack of resources or capacity to permanently identify dogs should not prevent the implementation of a vaccination campaign. The use of temporary coloured tags or plastic collars has proven to be useful in identifying vaccinated dogs and provided motivation for owners to take their pets for vaccination (Kaare et al., 2009).

Serological testing is often thought to be an alternative method for estimating vaccination coverage. However, for meaningful evaluations of titres, serological samples need to be collected within 1 month of vaccination campaigns, which is often logistically difficult, and the test should either be a WHO and OIE reference test (RFFIT (rapid fluorescent focus inhibition test) or FAVN (fluorescent antibody virus neutralization)), or have been calibrated against one of these reference tests. The minimum rabies virus neutralizing antibody titre of 0.5 IU per ml of serum (considered satisfactory for the international transfer of dogs and cats vaccinated at least twice under strict veterinary supervision) should not be used to assess vaccine efficacy in dogs immunized in the context of mass campaigns, in which lower values should be expected. Furthermore, the sheer numbers of animals that would need to be tested makes serological coverage assessments a very expensive and inefficient operation. Indeed, studies using serological and possibly other tests should only be considered if there is genuine concern about vaccine efficacy, as opposed to the quantitative assessment of levels of coverage attained.

Once rabies is eliminated, continued vaccination may be necessary in defined areas, depending on the risk of introduction, or for maintaining a cordon sanitaire from infected areas. Different strategies may be needed in vaccination campaigns designed to control infection in residual foci, or to contain new outbreaks.

#### Dog population management

In some communities the effectiveness of mass dog vaccination can be increased through dog population management. The need for dog population management should be evaluated at the beginning of a rabies control programme, through dogecology studies. As dog populations differ in demography, the collection of preliminary data on dog demography, dog ownership patterns, and community attitudes towards dogs is advised. This information can be used to determine the most appropriate manner for delivery of vaccinations and reproduction control. A combination of dog population management approaches is recommended, including responsible dog ownership, reproduction control, legislative measures, removal of dogs, and habitat management.

Contrary to popular belief that rabies can be effectively controlled by culling, considerable experience from projects around the world has found no evidence that removal of dogs alone has ever had a significant impact on dog population densities or the spread of rabies (WHO, 2005). There are several reasons for this:

**1.** Culling diverts resources from vaccination and takes considerable effort (often much more than vaccination), while generally only reaching a small proportion of the population.

**2.** Culling antagonizes communities and can lead to the movement of animals from infected areas where culling is taking place, which may often facilitate disease spread.

**3.** Culling may often be counterproductive, as sterilized, vaccinated dogs may be destroyed, therefore wasting resources.

A lack of options for permanent marking of vaccinated dogs means it is rarely possible to determine the vaccination status of free-roaming animals. Remaining dogs have greater resources and therefore populations recover rapidly, so any potential benefits of culling are short-lived. Even the highest recorded removal rates (about 15% of the dog population) are easily compensated for by increased survival rates (WHO, 2005). Culling may also increase demand for dogs by opening a market for replacement of culled animals. However, the targeted and humane removal of unvaccinated, ownerless dogs may be effective when used as a supplementary measure to mass vaccination. But in most developing country settings dog population control programmes tend to use methods that are considered unethical on animal welfare grounds (Dalla Villa et al., 2010).

The use of reproduction control for dogs can help to reach and maintain vaccination coverage. The rationale for reproduction control is to reduce the dog population turnover, the proportion of young dogs in the population, breeding behaviours that may make dogs more susceptible, and the number of ownerless dogs that may be more difficult to access for vaccination. Dogs may be accessed for reproduction control via their owners or by catching ownerless dogs from public areas, followed by sterilization and vaccination, post-operative care, and release at point of capture (Animal Birth Control, ABC, also known as catch, neuter, and release). Surgical sterilization is currently the most common method of reproduction control but is too costly to provide a sustainable solution to dog population management in all countries where this is required. Since the 1960s, ABC programmes coupled with rabies vaccination have been advocated as a method to control urban street dog populations and ultimately human rabies in Asia (Reece, 2007). In Jodhpur, an ABC programme that reached over 60% of the free-roaming dog population was found to both reduce and stabilize dog populations (Totton et al., 2010). Vaccination coverage has been predicted to remain above 70% if this programme is maintained, while surgical sterilization coverage of less than 40% would maintain the dog population at current levels (Totton et al., 2010).

#### **Future directions**

A major obstacle to effective dog rabies elimination is the rapid turnover in dog populations, and therefore the loss of herd immunity after mass vaccination campaigns. Surgical sterilization can be useful on a small scale for reducing turnover, particularly within targeted capture-neuter-release or ABC programmes for truly unowned dogs, but in many instances the cost of spaying/neutering very large numbers of animals is likely to be unsustainable (Menezes, 2008; Massei et al., 2010). The demand for sterilization techniques (both chemical and immunological) is therefore high. Some permanent sterilization options are under trial, for instance intratesticular injection of balanced zinc solution. While found to be safe and effective in Thailand and Mexico (Tepsumethanon et al., 2005; Esquivel-LaCroix, 2006), a study from the Galapagos reported side effects in a small proportion of dogs (Levy et al., 2008), and some concerns remain about the safety of this product. Considerable scope exists for the

development of safe chemical sterilization of both female and male dogs, which could substantially reduce the cost of current sterilization options. Immunocontraceptive vaccines seem, however, the most promising candidates for affordable and sustained dog population management. New immunocontraceptives are being developed, and research is under way to create a single injectable product such as a rabies vaccine-based recombinant immunocontraceptive (Rupprecht and Wu, 2009). Some are already registered for use in wildlife and will potentially become available at a fraction of the cost of surgical sterilization. Immunocontraceptives that induce fertility for 2–3 years will probably cover the entire lifespan of most dogs in the developing world (Kitala *et al.*, 2001). For example, Gonacon<sup>™</sup> (National Wildlife Research Center (NWRC) Animal and Plant Health Inspection Service (APHIS), US Department of Agriculture, Denver, Colorado; not registered, and not yet commercially available) administered in conjunction with a rabies vaccine does not affect parenteral rabies immunization in dogs (Bender et al., 2009), and so this contraceptive could be administered in conjunction with rabies vaccines to optimize dog population and rabies control.

Future research should focus on fieldtesting the feasibility, cost, and effectiveness of using immunocontraceptives to control dog numbers. By reducing the effort and costs of treating dogs, immunocontraceptives should reduce the costs of dog population management programmes. Future work should also address a number of other issues associated with immunocontraceptives, such as timing and frequency of applications in urban and rural areas, and public acceptance of fertility control in various cultural and social contexts (Massei and Meslin, 2011). Yet measures to promote responsible pet ownership including vaccination should not be forgotten, as they could go a long way to reducing the need for such tools.

Surveillance remains an enduring problem, and therefore increased deployment of field diagnostic tools and cheap and userfriendly means for reporting cases should be considered a priority. In general though, the obstacles remaining for effective rabies control are not technical (PRP, 2010). Effective tools are available, yet capacity and commitment to sustained implementation are lacking, despite the costs incurred for dealing with endemic rabies. Community engagement is not only critical for the success of vaccination campaigns and achieving necessary levels of vaccination coverage, but options for development of community-based sustainable initiatives could be further explored. A primary goal for the future is to find the means to increase local capacity for mass dog vaccination and humane methods of dog population control. Concomitantly, awareness must be raised at local, national, and regional levels to ensure that finances and human resources are effectively deployed. Intersectoral collaboration for rabies control is a major step towards this goal, but still remains an administrative and logistical barrier, and requires a shift in traditional thinking in many countries. Organization of campaigns based on intersectoral collaboration, community participation, strong media support, political commitment, acquisition and supply of canine vaccines by ministries of health, and free vaccine delivery has been key to success and sustainability in Latin America (Schneider et al., 2007). Similar approaches, once adapted to the local, national or regional context, could be equally effective throughout the developing world.

### **Cystic Echinococcosis Control**

Human echinococcosis is a neglected zoonotic disease resulting in a significant, though under-reported health burden globally, with >1 million lost disability adjusted human life years (DALYs) and a conservative estimate of 1.2 million cases annually (Budke *et al.*, 2006; Craig *et al.*, 2007; WHO, 2010c).

Two species of tapeworms of the genus *Echinococcus* are particularly important for public health, namely *E. granulosus* (sensu stricto) causing cystic echinococcosis (CE), and *E. multilocularis* causing alveolar echinococcosis (AE). Final or definitive hosts of both parasites are carnivores. However, the cycle of *E. granulosus* involves primarily domestic dogs as final hosts, and sheep, goats, camels,

cattle, and other livestock as intermediate hosts. Conversely, the cycle of *E. multilocularis* is predominantly sylvatic involving foxes and microtine rodents (see Chapter 8). The incidence of AE is relatively small (<20,000 cases annually) compared to CE, and mostly restricted to European and Eurasian foci, but pathological outcomes are more severe. This section will therefore concentrate on the control of cystic echinococcosis for which dog-focused interventions and surveillance are paramount.

E. granulosus is very widely distributed, involving most pastoral regions and especially sheep-rearing countries/regions of Australia and South America, including Argentina, Chile, Brazil, Peru, and Uruguay (Rausch, 1997). In Russia and parts of Eurasia, including Kazakhstan, Kyrgyzstan, Uzbekistan, and Mongolia, vast endemic areas exist. It has been recorded in 21 of China's 31 provinces and is one of the important zoonotic diseases in west and north-west China (Schantz et al., 1995; Craig, 2004). It also occurs throughout southern and eastern Europe, the Middle East (Jordan, Israel, Syria), and the Near East (including Turkey, Iraq, Iran, Afghanistan, Pakistan, India), with high transmission within the countries bordering the Mediterranean, the Black Sea, and on the Iberian Peninsula (WHO/OIE, 2001). In Africa, two major endemic zones exist, including countries of the north (Morocco, Algeria, Tunisia, Libya, Egypt) (Kachani et al., 1997) and in East Africa (Kenya, Uganda, Tanzania, Sudan, Ethiopia) (Macpherson et al., 1989).

Major risk factors for contracting human CE are represented by direct and indirect contacts of humans with faeces from infected dogs. Children are often found infected, because of their close contacts with dogs or with environments/food contaminated by dog faeces. In endemic areas, such as Mediterranean countries, eastern Africa, South America, and western and central China, cysts may be found in 1–40% of cattle and 1–80% of sheep, and from 0.2% to 50% of dogs are infected. In humans, the parasite occurs as a benign tumour (hydatid cyst), unique or multiple, in the liver or lungs, in most cases. However, any tissue or organ may be involved, including brain, bone, spleen, and kidney. After a silent asymptomatic period, various symptoms and signs are observed, depending on the primary location of the cyst(s). Rupture of the cyst may lead to life-threatening anaphylactic shock and to dissemination to many tissues and organs. Treatment is represented by surgery, interventional radiology (puncture and sterilization of the cysts), and benzimidazole drugs, or a combination of treatments (Brunetti et al., 2010). Depending on the area considered, annual incidence of human CE surgical cases in endemic countries ranges from 1 to 200 per 100,000 inhabitants. However, in highly endemic foci of some countries, community mass screenings with abdominal ultrasound have shown local prevalences of 5% to >10% (Macpherson et al., 1989; Li et al., 2010). However, cystic echinococcosis is theoretically an eradicable disease, and success in elimination of regional and local transmission of human CE disease has been achieved (WHO/OIE, 2001; Craig and Larrieu, 2006).

## Historical perspective of echinococcosis control and the island programmes

The life cycle of the tapeworm *Echinococcus* granulosus was determined by European scientists during the 1850s as a result of the independent research of von Siebold, Naunyn, Krabbe and others (Grove, 1990). This new knowledge identified parasite transmission with dogs as definitive host of the adult worms, and livestock/herbivores as intermediate hosts of hydatid cysts. This immediately led to the development of detailed recommendations for 'hydatid control' in the early 1860s. Control was recommended to be based on four aspects: (i) prevent dogs having access to livestock offal; (ii) treat dogs with an anthelmintic; (iii) meat inspection and offal disposal; and (iv) health education about the parasite lifecycle, hygiene, and dog contact. These components were articulated in the 19th century but are still valid today (WHO/OIE, 2001; Craig and Larrieu, 2006). Consequently in the 20th century hydatid control programmes at national or state/

regional level were eventually successfully implemented in five island regions (Iceland, New Zealand, Tasmania, Falkland Islands, Cyprus) (Gemmell and Roberts, 1998).

## Echinococcosis control in Iceland (from 1864)

The Danish veterinary scientist Harald Krabbe was posted to Iceland in 1860 where human hydatid disease (cystic echinococcosis) was highly prevalent among the Icelandic population (up to 22% autopsy prevalence). In 1864 he wrote an 18-page information booklet in Icelandic Scandinavian that was distributed free to all households, about the life cycle of the hydatid parasite and the role of dog management and livestock slaughter practices in disease prevention. A Hydatid Law, first passed in Iceland in 1869 (and expanded in 1890, 1924, 1953, and 1957), imposed a tax on dog owners. It became illegal to feed livestock offal to dogs, infected organs had to be burnt or buried, and dogs were to be treated annually by a designated village 'dog-cleaner' with an areca seed extract vermifuge (replaced in 1930 by arecoline hydrobromide) (Beard et al., 2001). Reduced transmission was also facilitated by reduction in dog numbers as a result of several distemper epidemics between 1870 and 1892, and from 1870 livestock husbandry changes were made from primarily wool and milking ewes to fat lamb production with export of adult sheep. By the decade 1890-1900 new cases of human CE were rare in Iceland. In the 36-year period 1930-1956, 3576 human autopsies were performed and of these 130 (3.6%) were found to be infected with CE, the highest prevalence occurring in patients aged over 60 years (n=57) born in the period 1841–1880 (Dungal, 1957).

The last transmission between dogs and humans in a non-latent autochthonous case in Iceland was diagnosed in 1960 in a 23-year-old woman (Beard, 1973). Ovine CE prevalence in Iceland for the period 1948–53 was 0.0008%, with the last confirmed sheep infections in 1973. Surveillance through meat inspection was maintained during the 20th century, together with annual dog treatment (with praziquantel (PZQ) from 1979) and the application of strict importation regulations (Beard et al., 2001). Iceland has been considered free of *E. granulosus* since the 1970s, after previously (1880s) having the highest national prevalence ever recorded worldwide. The Iceland hydatid campaign was the first in the world, and succeeded, in large part through health education, to eliminate parasite transmission and human CE from the country. Though elimination took more than 100 years, human CE incidence fell dramatically within 30 years of the distribution in 1864 of Krabbe's booklet on E. granulosus and hydatid disease. Educational programmes, however, without a vertical control effort directed against dogs, have not been successful in reducing CE transmission in other regions of the world (Craig and Larrieu, 2006).

## Echinococcosis control in Australasia (from 1959)

*E. granulosus* and human CE remain endemic in mainland Australia, especially in eastern regions (Gemmell, 1990; Jenkins, 2005). Human CE, however, was also formerly an important public health problem in New Zealand and Tasmania, but both island territories declared that hydatid disease was eliminated from their islands by 2002. This was the result of wide-scale well-organized government-backed hydatid control programmes implemented between 1959 and 1997 (New Zealand) and 1964 and 1996 (Tasmania) (Craig and Larrieu, 2006).

Human CE in New Zealand was recognized as a public health problem towards the latter part of the 19th century and was made a notifiable disease in 1873; emphasis was also placed on health education (as was done in Iceland). Intensified health education from 1938 to 1958 also provided free arecoline for owners to dose their dogs every 3 months, and the 1940 Meat Act made it illegal to feed raw offal to dogs. However, despite this health education approach, in the late 1950s nearly 50% of sheep remained infected, including >80% of sheep ranches surveyed, and human CE incidence in rural areas was 11.8 surgical cases per 100,000 (Gemmell, 1990). As a result, a National Hydatid Eradication Council (Hydatid Act 1959) was formed, with local authorities applying the day-to-day control measures; this was funded through a local dog tax added to the normal dog licence fee. Overall this 'attack' phase lasted about 32 years (1959–1991) and initially involved supervision of dog registration and the application of arecoline hydrobromide by technicians to detect dogs infected with E. granulosus (or Taenia hydatigena), and to penalize owners. Dosing was applied up to four times yearly over 13 years (1959-72), and later under the more effective direction by the Ministry of Agriculture through 6-weekly dosing (niclosamide initially then PZQ after 1978). During this period in New Zealand, transmission of E. granulosus from dogs to humans virtually ceased (Meslin et al., 2000) and the national ovine CE prevalence by 1980 was only 0.43%. In 1990 movement control of livestock and slaughterhouse surveillance (including diagnostic histology for very small lesions) with trace-back was introduced as key elements of a 'consolidation' phase of control after dog dosing had ceased. A 'maintenance of eradication' phase was reached in New Zealand in about 1998 and consisted of permanent surveillance of livestock at meat inspection, together with restrictions to re-entry of the parasite in livestock (Gemmell and Lawson, 1986; Gemmell, 1990).

The Australian island State of Tasmania adopted a very effective hydatid control programme (1964–1996) at a time when human CE incidence was >25 per 100,000 in the rural population. The Tasmanian programme differed in four important aspects from the New Zealand hydatid control scheme, which resulted in a shorter 'attack' phase (11 years in Tasmania versus 32 years for New Zealand) (Craig and Larrieu, 2006). These were: (i) funding and management was by the Department of Agriculture from the outset; (ii) mobile dog testing/purgation (with arecoline) units were used to visit farms annually (with added value for educational aspects), rather than purge samples being sent to a central testing laboratory (as was done in New Zealand); (iii) dog testing was confined to rural dogs only; and (iv) farms

with positive dogs were quarantined under strict State legislation (Beard *et al.*, 2001). No human CE cases occurred in the under-20 years age group in Tasmania after 1976; ovine CE prevalence reduced from 52% to 3.4% in older sheep by 1978, and dog prevalence dropped from >12% to 0.06% by 1981–85 (Beard *et al.*, 2001). Two small outbreaks of CE in local livestock have occurred in Tasmania since 1990, in 1997 and in 2009. Both may be associated with import of infected dog(s) from the mainland (D. Jenkins, pers. comm.).

# Echinococcosis control in the Falkland Islands (from 1965) and Cyprus (from 1971)

CE was first recorded in the Falklands in a sheep in 1941 (probably introduced), but by 1969 slaughter records showed a prevalence of 59% (Whitely, 1983). The first local human CE cases were recorded in 1963 with an equivalent annual incidence of 55 cases per 100,000 for the period 1965–75 (Bleany, 1984). Hydatid disease control was introduced in the Falklands in 1965 (Tapeworm Eradication Dogs Order). This order made provision for: (i) the appointment of dog inspectors; (ii) the purging of dogs with arecoline acetarsol (Tenoban); and (iii) prohibiting the feeding of raw offal to dogs. From 1970, under a second Tapeworm Eradication Order, dog-dosing was undertaken every 12 weeks with bunamidine hydrochloride and from 1977 was replaced with PZQ every 6 weeks. Drugs were paid for by owners initially, then PZQ was provided free; dosing continued at least until 2011. Strong reliance was also placed on offal disposal and confinement of dogs unless being worked. Legislation was updated by the Hydatid Eradication (Dogs) Order 1981. By 1981 ovine CE prevalence was 1.8% and further reduced to 0.16% in 1993 (Reichel et al., 1996). Unfortunately no pre-control dog data exist. The only dog prevalence data refer to coproantigen ELISA testing done in 1992-3 when 1.7% of 464 dogs were positive (Reichel et al., 1996). The last human CE case (old case) was reported in 1992 (S. Ponting, pers. comm). In the Falklands, several permanent measures remain in place, which have

kept echinococcosis at very low transmission or district level elimination. These include: (i) a national dog registration scheme with notifications of transfer to new owners, births, and deaths to the Department of Agriculture; (ii) coproantigen tests applied periodically to dog populations; (iii) retention of 6-weekly supervised dog treatment with PZQ; and (iv) retention of safe offal disposal and surveillance through meat inspection and restrictions to parasite re-entry (Gemmell and Roberts, 1998; S. Pointing, pers. comm.). In 2010 a suspect hydatid cyst in a 7-year-old sheep was confirmed by DNA analysis to be *E. granulosus* (sheep G1 genotype), and only 2/563 (0.004%) of dog faecal samples were coproantigen positive, including one dog positive for E. granulosus copro-DNA (S. Ponting, B. Boufana, P.S. Craig, unpublished).

In the 1960s, the annual surgical CE incidence on the island of Cyprus was 12.9 per 100,000; ovine CE prevalences ranged from 25% to >80% in aged ewes, while 14% of farm dogs were infected (Economides et al., 1998). A national hydatid control programme was introduced into the Republic of Cyprus in 1971 under the Ministry of Agriculture. The intervention emphasis (i.e. attack phase) was primarily focused on the reduction/elimination of stray dogs (85,000 killed between 1971 and 1985), and obligatory field-testing with arecoline every 3 months for registered owned dogs, with euthanasia of all E. granulosus purge-positive dogs (Polydoru, 1993). A public health education programme was also instigated, together with strict slaughter controls and meat inspection (Economides et al., 1998). Total dog prevalence reduced from 7.4% to 0.75% by 1977 and by 1984-5 zero (0/36,000) dogs were infected after arecoline testing; in addition, no human CE cases under 20 years of age were diagnosed. It should be noted that after 1974 the campaign was continued only in the area controlled by the Government of the Republic of Cyprus. Eradication was claimed in 1985, with cessation of activities in the Government Controlled Area (GCA) (Polydorou, 1993). Following a reappraisal in 1993–1996, however, it was found that the parasite was still present sporadically in livestock in 21% of villages and in 0.6% of dogs purged in the GCA.

Furthermore, a coproantigen ELISA survey in 1997-2000 revealed 2.8% positives in >6500 dogs tested in the GCA, with an 8.1% coproantigen prevalence in dogs surveyed from Northern Cyprus (non-GCA) (Christofi et al., 2002). In order to prevent a re-emergence of human CE, measures were reapplied from the mid-1990s by the Department of Veterinary Services that included: (i) treatment of all dogs with PZQ 2-3 times per year; (ii) elimination of stray dogs; (iii) movement control of all animals; and (iv) prosecution for illegal slaughtering. Release from farm quarantine was applied only after at least 3 years absence of E. granulosus or T. hydatigena cysts at meat inspection (Economides et al., 1998; Economides and Christofi, 2002).

## Success of island hydatid control programmes

All five 'island programmes' were successful in significantly reducing or eliminating human CE as a public health problem. The programmes themselves and their duration differed. The Icelandic programme, which from the 19th century was largely based on health education and general improvement in livestock husbandry and dog management, required about 110 years. In contrast, the hydatid control programmes of New Zealand, Tasmania, the Falkland Islands, and Cyprus, which all eventually or immediately targeted the dog population, required 10–30 years for human CE incidence to become negligible. With respect to differences in the duration of the 'attack' phase between New Zealand and Tasmania (34 and 11 years, respectively), this was in large part due to differences in control structure. The former involved a Hydatids Council with local authorities employing technicians to dose dogs with a centralized national testing station to identify infected dogs, and was only later under the direction of the Ministry of Agriculture. In contrast, in Tasmania, technical officers of the Department of Agriculture tested dogs directly on site for evidence of infection, using mobile laboratories, and then quarantined farms with infected dogs.

The Falklands programme used Department of Agriculture-supervised dog dosing with PZQ from 1977 and has maintained this to the present (2011) (i.e. 34 years in a PZQbased attack phase). In Cyprus, from 1971 a draconian stray dog elimination scheme coupled with an owned-dog arecoline testing programme (with euthanasia of positive dogs) rapidly reduced transmission within 10 years. The Department of Veterinary Services in Cyprus subsequently re-applied strong 'consolidation' measures based on livestock surveillance and quarantine from 1993.

# Options for echinococcosis control programmes

In the second half of the 20th century, other hydatid control programmes were initiated following the success of the Australasian, Falklands, and Cyprus island programmes, that were to virtually eliminate human CE as a public health problem. At least seven other control programmes of variable duration, impact, and success, were activated by the 1980s in 'continental' regions, that is, within Argentina, Chile, Uruguay, Brazil, Spain, Wales, and Kenya. Dr Michael Gemmell, based in New Zealand from the 1960s and closely involved with their national hydatid control programme, assessed and reviewed all the Island programmes. This enabled him to formulate five 'Options for Control', and in parallel he described four phases of implementation for hydatid control programmes (Gemmell, 1990; Gemmell and Roberts, 1998). These options were further outlined by Craig and Larrieu (2006).

 Option 1: Decision not to proceed. For example, because human CE is not a priority public health issue, such health data are not available, suitable control structure and funding are not available, or there are unfavourable epidemiological features (e.g. an under-developed region with dispersed population and no abattoirs). Decision may be temporary until the situation/priorities change.

- Option 2: Implementation of a long-term 'horizontal' approach involving health education, upgrading of abattoirs and meat inspection, with reliance on owners to treat dogs with free wormer (e.g. Iceland and New Zealand programmes; required 30–100 years).
- Option 3: 'Vertical' long-term approach incorporating at least annual on-site arecoline purge testing of dogs by veterinarians with associated education of owners, and resultant on-property quarantine of *Echinococcus*-positive dogs (e.g. Tasmania; 15–30 years).
- Option 4: Vertical 'fast-track' approach, based on elimination of stray dogs and euthanasia for arecoline test *Echinococcus*positive owned dogs (e.g. Cyprus; 10–15 years).
- Option 5: Vertical 'fast-track' approach with specified regular (usually 4, 6, or 8 times per year) treatment of all registered dogs with PZQ (e.g. New Zealand after 1990, Falkland Islands after 1977; 10–15 years).
- Option 6 was additionally recommended (Craig and Larrieu, 2006) as a 'fast-track' approach based on a specified lower frequency of PZQ dog dosing (e.g. 2–4 times per year) in parallel with vaccination of sheep (using EG95) against *E. granulosus*. However, to date (2010–11) this strategy has been modelled but not yet fully/ adequately implemented in a specified CE-endemic region.

## Successful and problematic hydatid control programmes in continental regions

## South American hydatid control programmes

From the early 1980s, hydatid control programmes based on the systematic supervised dosing of dogs with PZQ were implemented in South America in regions of Uruguay, Chile, and Argentina, with distinct organization models for the Control Authority. In Uruguay they opted for a 'New Zealand-style' Honorary Hydatids Commission under the jurisdiction of the Ministry of Public Health; Chile opted for the Ministry of Agriculture (similar to programmes in Tasmania, Cyprus, and the Falkland Islands), while in Argentina the Ministry of Health was the overall control authority. With minor local differences, hydatid control activities (since the late 1990s) in South America have been based on:

- registration and PZQ treatment of dogs at the dose of 5 mg/kg every 6–8 weeks;
- accompanying health education;
- slaughter control to prevent access of dogs to viscera;
- legislation for the regulation of dog populations; and
- recommendations for construction of basic infrastructure in cattle and sheep ranches/estancias comprising designated slaughter area, and pit for disposal of infected viscera.

The Chilean hydatid control programme in Region XII was very successful from the outset with evidence of reduction in E. granulosus transmission in the first 5 years (from 1979). The Neuquén Province (Argentina) pilot programme from 1970 resulted in significant control and cessation of new human CE cases after 17 years. In contrast, the Uruguay national hydatid control programme had little effect on either livestock or human CE rates over the first 20 years of the control campaign (1972-1992) when it was based on arecoline testing, and importantly failed to reach more than 60% of rural dogs. Thereafter from 1994, and similar to Chile and Argentina, a 6-weekly dosing programme with PZQ and a higher dog population cover, drove canine prevalence to < 1%in Uruguay by 2002 (Table 12.2).

In Region XII (Chile), ovine CE prevalence had declined from >60% to 25% in sheep (with 1% in lambs), and canine echinococcosis prevalence was reduced to 1.6% within 5 years (1979–1984) of implementation of PZQ dog dosing for hydatid control (Table 12.2). Human CE incidence also decreased from >40 per 100,000 per annum to 19.6 per 100,000 by 1984, and reduced further to 11.8 per 100,000 by 1992 (Gemmell and Roberts, 1998; Craig and Larrieu, 2006). The 'attack' phase in

Outcome (% or inc					or incid.) y	d.) years		
Programme	Dates	Option <sup>a</sup>	approach	screen	Pre	10	<20–30	>30
Iceland	1863–1960	2	Education	Autopsy	22			(5.9, 1.5, 0)
NZ	1959–1997	(2) 5	Education, PZQ	Ovine	48–58		04–15	1×10 <sup>-6</sup>
				Dogs	37		<5	0
Tasmania	1965–1996	3	Education,	Ovine	52.2	8.7	0.6	0.0002
			Arec, Quarn					
				Dogs	12.7	0.8	0.06	
Cyprus	1971–1985	4	Culling Arec	Dogs	6.8	0.02	0.17	2.6
				Ovine	66	0.9	0.014	
Rioja	1987–2000	5	PZQ, culling	Ovine	82.3	20		
				Dogs	7	0.2		
Uruguay	1994–2002	(3) 5	Arec, PZQ	Ovine.	41	9		
				Dogs	10	0.7		
Rio Negro	1980–1997	5	PZQ	Dogs	41		2.9	
				Ovine	61		18	
Region XII	1982–1997	5	PZQ	Ovine	60–80	25	5–7	
				Dogs	71	1.6		
Rio Grande	1983–2000	5	PZQ	Ovine	26		3	
				Dogs	28		9	
Wales	1983–1989	5	PZQ	Ovine	23.5	10.5		
			Arec, CopAg	Dogs	4.6–25	0	9	

Table 12.2. Island control programmes for cystic echinococcosis (CE) (After Craig and Larrieu, 2006).

NGA = non-government controlled area; Arec = arecoline; PZQ = praziquantel.

Chile Region XII lasted a total of 18 years (1979–1997), but from 1987 dog dosing was reduced from eight times per year to twiceannual treatments in order to save on costs and improve logistics. However, in 1991 the Chilean Ministry of Agriculture re-introduced the eight treatments per year schedule (half by dog owners themselves) in Region XII in order to further reduce transmission to sheep which had plateaued at a prevalence of 5-7% after 1986 (Gemmell, 1997). Within 3 years of the increase in dog-dosing frequency from 2 to 8 times per annum (>90% dogs were treated), the prevalence of E. granulosus in dogs and lambs in Region XII was reduced close to zero by 1994 (Craig and Larrieu, 2006).

#### European hydatid control programmes

At least three hydatid control programmes in which dogs were primarily targeted, were undertaken in endemic areas of Western Europe from the 1980s, in La Rioja, Spain (1987-2000); mid-Wales, United Kingdom (1983–1989); and Sardinia, Italy (1987–1997). These intervention programmes included the requirement of registration and regular dosing of owned dogs with PZQ as the key intervention tool. In that regard they can be considered to have adopted Option 5 (see above) as a relative fast-track vertical control programme. Supervised dog dosing with PZQ was implemented at eight times per year in two of the three regions, though this was only maintained for the first 6 years in La Rioja and mid-Wales; nevertheless it was able to reduce canine echinococcosis prevalence by >90% and ovine CE prevalence by 50-75% (Palmer et al., 1996; Jimenez et al., 2002). Despite an accompanying strong health education component the Sardinian programme was poorly accepted by rural sheep farmers, as was the control authority and its operatives (the Sardinian Experimental Institute for Zooprophylaxis was the agency involved), and the programme did not significantly reduce either dog or ovine prevalences of E. granulosus over 10 years (Conchedda et al., 2002).

The La Rioja hydatid programme was managed under the Ministry of Health.

stray/unwanted Significant dog populations in La Rioja and Sardinia were considered an important reservoir of E. gran*ulosus*, but became a difficult issue for public acceptance in relation to implementation of mass euthanasia. Euthanasia of stray dogs, apart from reducing the potential transmission reservoir, also provided availability of necropsy-based dog data on E. granulosus prevalence. In La Rioja 500–1000 stray dogs per annum were examined post-mortem and showed a prevalence reduction from 7% to 0.2% after 10 years of dog dosing (Jimenez et al., 2002). In Sardinia, by contrast, euthanasia was replaced early in the programme by legally binding legislation for municipalities to impound and treat stray dogs indefinitely; this became unsustainable, and contributed, along with poor anthelminthic coverage of owned farm dogs, to the failure after 10 years of the (well-funded) Sardinian hydatid control programme (Craig and Larrieu, 2006).

As for La Rioja, the mid-Wales hydatid control programme (1983–89) involved 6-weekly supervised PZQ dosing of owned farm dogs (in this case by Ministry of Agriculture veterinarians), the construction of burial pits/metal containers for safe disposal of sheep carcasses, and widespread health education in local communities and schools. Ovine CE prevalence for sheep from the Welsh control zone reduced from 23.5% to 10.5% within a 3-4 year period. Arecoline purge prevalence of canine echinococcosis in the 1970s prior to control, ranged between 4.6-25% in farm dogs (Walters and Clarkson, 1980). After control measures were prematurely disbanded in 1989 due to budget considerations, the effect of 5 years of PZQ dosing on canine echinococcosis prevalence was measured using a laboratory-based faecal test for detection of Echinococcus coproantigens (copro-ELISA) (Craig et al., 1995). Canine coproantigen prevalence in the control zone was 0% in 1993, but had increased to 6.3% (by 1996) and reached a plateau at 8-9% from 2002 to 2008 (Palmer et al., 1996; Buishi et al., 2005a; Mastin et al., 2011).

## Hydatid control in nomadic pastoral communities

Human CE is a common, though underrecognized public health problem in many of the world's nomadic or semi-nomadic pastoral societies (Macpherson, 1994; Zinsstag et al., 2005). These communities inhabit marginal lands with low rainfall (e.g. arid zone Nilotic tribes in East Africa) or low seasonal temperatures (e.g. alpine grasslands of Tibetan, Mongolian, Kazakh pastoralists). Both humans and their livestock populations are interdependent, and are almost always associated with dog ownership for practical value (i.e. herding, guarding, hunting, scavenging) and companionship, but almost never for human food. Nomad groups are usually geographically isolated and have poor access to health, veterinary, and education services, and are also fiercely independent with characteristic disdain for formal government organization and their operatives. This makes it particularly difficult to implement, manage, involve community participation, and to monitor progress in hydatid control in such pastoralist societies.

In the Nilotic Turkana tribe in northwest Kenya, human CE surgical incidence was more than 200 per 100,000 per annum and hepatic CE prevalence by ultrasound from 5% to 9%. From the start in 1983 of a Turkana-based pilot control scheme against CE, administered by the African Medical and Research Foundation (a non-governmental organization, NGO) (Macpherson *et al.*, 1984), difficulties included:

- virtually no educational, medical, or veterinary facilities;
- poor communications, and road network with few settlements;
- no abattoirs;
- a population of nomadic and largely illiterate indigenous people;
- occurrence of frequent droughts; and
- commonplace inter-tribal livestock raiding and fighting (Macpherson and Wachira, 1997).

Despite these inherent problems, hydatid intervention attempted to comprise elements of Option 4 (i.e. dog culling, bitch sterilization, and health education) and Option 5 (specified 6-weekly treatment of dogs with PZQ) (Craig and Larrieu, 2006). Mobile teams visited village clusters as well as temporary nomad encampments (manyattas). The 'attack' phase based on PZQ dosing of dogs eight times per year was maintained for the first 2 years, then for logistic reasons was reduced to 3-4 times per year or less. The campaign operated 'on and off' for about 10 years (1983-1994). However, difficulties in transport and manpower, and under-funding meant that only about 30% of dogs were registered in the first 2 years, and of those only between 30-60% were followed up regularly for PZQ treatment (Macpherson et al., 1986; Macpherson and Wachira, 1997). Due to absence of livestock data, surveillance was based on dog and human prevalence surveys, using necropsy of unwanted dogs and arecoline testing of owned dogs, together with mass ultrasound abdominal scanning for human CE. Within 5 years of the start of the hydatid control pilot in northwest Turkana, human CE prevalence based on ultrasound scanning reduced from >7% to <4%, with very few cases in the under-5 years age group. Human prevalence then appeared to plateau around 3% after the mid-1990s (Craig and Larrieu, 2006). Prevalence estimated by necropsy of unwanted dogs reduced from 63% to around 45% within 5 years, and was 27% after 11 years (1983–94) (Macpherson and Wachira, 1997). An Echinococcus coproantigen survey of owned dogs in the Turkana Control Zone in 2002 showed that coproprevalence (31%) was still high, though average worm burden was significantly reduced (Buishi et al., 2006).

Investigations from the mid-1990s showed that human CE prevalence in Tibetan seminomadic pastoral populations living on the eastern Tibetan Plateau (located 3500–4500 m altitude in Sichuan and Qinghai Provinces, China) ranged from 1% to >15%, and were among the highest ever recorded worldwide (Schantz *et al.*, 2003; Li *et al.*, 2005, 2010). In Datangma district, Ganzi Tibetan Autonomous Prefecture (Sichuan Province) a pilot hydatid control scheme was implemented from 2000 to 2005 and included twice-yearly PZQ dosing by owners of their dogs (and a proportion of accessible strays), together with health education. Planned dog dosing six times per annum was found to be unworkable due to the severe winters. An attempt was also made to use an anti-CE vaccine (EG95) in sheep and yaks with annual boosters. Surveillance, similar to Turkana (Kenya) described above, was based primarily on coproELISA testing of dogs and necropsy of unwanted dogs, because formal slaughter houses did not occur (Yang et al., 2009). In addition human screening by ultrasound was implemented. An additional complication in this region was the high coendemicity of E. multilocularis in dogs which caused an equal or higher community prevalence (compared to CE) of human alveolar echinococcosis (AE). After 5 years of twiceannual dog dosing, Echinococcus spp. coproE-LISA prevalence in owned dogs reduced significantly from 50% to 17%, but a significant reduction did not occur in necropsy data for stray dogs (Yang et al., 2009). Around 25% of this Tibetan community did not readily accept dog dosing or livestock vaccination, and therefore the percentage of animals treated or vaccinated was never more than 30%. In addition, serological testing of livestock to measure EG95 antibodies revealed that at least 50% had not been vaccinated, or allowed the vaccination of livestock, as planned.

There are huge difficulties in attempting to control the transmission of cystic echinococcosis in nomadic or semi-nomadic pastoralist communities. Nevertheless, human CE is of major public health importance in these groups and should be targeted by health and veterinary authorities. One possible answer to the problem is to develop an integrated approach to strengthen both human and animal health systems ('One Medicine'), which could more costeffectively bundle together several zoonotic (e.g. CE, rabies, brucellosis, human, and bovine TB), and non-zoonotic diseases (e.g. vaccinepreventable childhood infections), and also lead to better outreach and acceptance by pastoralists (Zinsstag et al., 2005).

#### Planning and implementation of CE control

The decision to reduce incidence of human CE is usually made by a public health authority after consideration of hospital treatment records or data from mass screening surveys. Implementation of a hydatid control programme may then be considered, and may be facilitated by a Ministry of Health, a Ministry of Agriculture, a Department of Veterinary Services, a local Municipality, an Honorary Hydatids Commission, or an NGO. There may also be cooperation or collaboration between the various authorities, such as those managing public health and veterinary aspects. Hydatid control has been recommended to be broadly divided into four phases (Gemmell and Roberts, 1998; WHO/OIE, 2001; Craig and Larrieu, 2006). These are outlined below.

#### Preparatory or planning phase

- Assess the quality of baseline data on human and livestock CE incidence and prevalence, and canine echinococcosis prevalence.
- Assess the public health impact of human CE and its priority for regional public health.
- Calculate the economic losses due to livestock and human CE.
- Identify the control authority, including its legislative powers and funding commitments (preferably long term).
- Consider whether transmission is significant enough to designate CE as a notifiable disease at national or provincial/ regional level.
- Undertake a cost–benefit analysis for control and of the different control options (e.g. horizontal versus vertical approaches; Options 1–6 above).
- Consider the role of education for local needs/knowledge/socio-cultural aspects.
- Identify key staff and needs/training (veterinary and technical staff, medical advisors, quantitative epidemiologists, etc.).
- Establish cooperation with local/rural groups (e.g. voluntary farmers' unions, livestock herders).
- Assess operational research needs and logistics, and establish the feasibility of data collection and potential quality/ reliability of surveillance data.

- Identify liaison avenues between the control authority, the Ministry of Agriculture/Department of Veterinary Services, the Ministry of Health, the Municipalities, and if appropriate specific government, university, or NGO research/health agencies.
- Consider whether CE control can be integrated for improved cost-benefit with control of other important zoonoses and infectious diseases in general (planning phase needs 1–2 years).

#### Attack phase

- Control measures against *E. granulosus* are applied, principally to involve dog registration, and then specified regular mass treatment 4–8 times per year with PZQ of the entire owned rural dog population (or >90%), ideally by trained operatives.
- Reduction in stray dog numbers if a problem, and/or PZQ baiting of stray dogs.
- Parallel health education about hydatid disease, the parasite life cycle, safe disposal of livestock offal, and participatory acceptance of the control programme itself at community and school levels.
- Set-up of abattoir/slaughter slab surveillance for specified areas, and also a dog-surveillance approach (arecoline purgation and/or coproantigen testing; necropsy of unwanted dogs).
- Possible application of anthelmintics for livestock, for example oxfendazole.

This is the most costly phase in terms of expenditure and manpower and therefore should be as short as possible. A reduction in dog infection prevalences should be significant within 1 year, livestock (sheep) within 5-7 years, and human CE rates (<15 years age group) within 10 years. Transmission to dogs will only cease after 1-2 generations of sheep has elapsed. If feasible, removal of old sheep (>10 years) with compensation should be implemented. Results of the intervention should be communicated to relevant veterinary, health, and municipal authorities; an annual decision should be made to continue ('attack' phase usually requires 10-15 years).

## Consolidation phase

This phase occurs after dosing dogs in the attack phase has ceased, because of positive intervention surveillance indicators (i.e. dogs, livestock, humans). It involves:

- proactive identification of infected food animals at abattoir meat inspection, ideally with trace-back ability;
- possible use of enforced dog treatment and legislation to quarantine affected and neighbouring properties (with a specified period free from CE and possibly also *T. hydatigena*);
- possible provision of PZQ to dog owners free or at low cost, and random surveillance of dogs by coproantigen tests or arecoline purge testing;
- possible use of sentinel lambs and/or cattle to assess exposure, particularly if centralized slaughter records are difficult to obtain;
- possible prosecution for illegal slaughtering (if appropriate);
- possible recommendation to remove old sheep.

This is a long-term phase after the expensive 'attack' phase, and should require a reduction in field staff and the cost of anthelminthics (consolidation phase needs >20 years and may need to be more or less permanent in continental programmes).

#### Maintenance of elimination phase

In this phase, specific control activities have stopped and active consolidation reduced. However, vigilance should be maintained through meat inspection, and measures applied to prevent entry of infected animals such as dogs or livestock through use of a licence or passport (this is easier on islands). The ability to trace back from abattoirs, and to control limited outbreaks on specified infected properties should be maintained or initiated. The definition of elimination or eradication of E. granulosus for a specified territory becomes an important issue. This is a permanent phase, but it may be required to readopt broad consolidation measures if re-emergence of transmission occurs (as occurred in Cyprus, New Zealand, and mid-Wales, for example, in the 1990s).

## Control tools and surveillance for echinococcosis

#### Canine echinococcosis

Post-mortem examination of dogs is the gold standard for detection of the adult tapeworm of *E. granulosus*, but such an approach can usually only be applied for surveillance using stray or unwanted dogs (and may be facilitated in cooperation with rabies control). Arecoline is a strong purgative that may eliminate a large proportion of gastrointestinal worms, including Echinococcus, and therefore is used as an ante-mortem diagnostic test if purges are examined. The great advantage of arecoline is that it should be 100% specific, and purgation also can provide an important on-site educational tool for dog owners. Arecoline sensitivity for E. granulosus is normally only around 70% and up to 25% of dogs fail to purge; it may also be stressful for dogs, is potentially biohazardous for operatives, is difficult to implement, and is labour-intensive (Craig, 1997). Despite these drawbacks, until the mid-1990s arecoline purgation was the only reliable and practical test for canine echinococcosis. It was used to great effect in several hydatid control programmes, especially notably those carried out in Tasmania, New Zealand, and Cyprus, where hundreds of thousands of dogs were arecoline tested (Craig and Larrieu, 2006). The widespread availability of the anthelmintic PZQ from the 1980s replaced the reliance on arecoline purgation as the main tool of the 'attack' phase. PZQ, with its very high efficacy, was evaluated in the 1970s and found to be highly effective (>98%) by both oral and intramuscular routes against E. granulosus and E. multilocularis at a single dose of 5 mg per kg (Gemmell and Johnstone, 1981).

The development in the early 1990s of a highly genus-specific coproantigen ELISA provided the first useful laboratory test for the ante-mortem diagnosis of canine echinococcosis (Allan and Craig, 1989; Allan *et al.*, 1992; Deplazes *et al.*, 1992). Coproantigen testing can be performed on fresh, frozen, or formalin-preserved faecal samples, collected per rectum or from the ground. Comparison of the coproantigen ELISA with necropsy or arecoline purge indicated specificity of 91-98% and sensitivity of 62-100% (Craig et al., 1995; Lopera et al., 2003; Buishi et al., 2005b). Test sensitivity was more variable with low worm burdens (< 50–100 worms), but was able to detect pre-patent juvenile infections by 2wpi (weeks post infection), and dogs became copro-negative within 4-5 days post treatment (Allan et al., 1992; Craig et al., 1995; Jenkins et al., 2000). Coproantigen detection was also shown to be superior to serological diagnosis of canine echinococcosis, mainly because of the poor correlation of serum antibodies with current infection (Craig et al., 1995). Coproantigen ELISA has already been used for surveillance purposes in at least four hydatid control programmes, namely the Falkland Islands, Cyprus, mid-Wales, and Tibetan Sichuan (China). In the Falkland Islands in the mid-1990s the test was used to screen about 50% of the dog population in order to identify the remaining foci of infected sheep farms; 1.7% of dogs were coproantigen-positive (Reichel et al., 1996). By 2010 the coproantigen prevalence in Falklands farm dogs had reduced to 0.004% (n=563) (S. Ponting, B. Boufana, P.S. Craig, unpublished). Similarly, in Cyprus > 6500 owned dogs were screened between 1997 and 2000 in the consolidation phase of hydatid control. Of these, 2.8% were copro-positive in a low prevalence zone, and copro-positive dogs were treated with PZQ (Christofi et al., 2002). Coproantigen testing of farm dogs in mid-Wales was employed to assess the impact of a 6-year hydatid control programme (1983–89). Coproantigen prevalence in Welsh farm dogs was 0% in the control zone 4 years after cessation of supervised dog dosing. However, 13 years after the attack phase, coproantigen prevalence had increased to 8%, signalling a potential re-emergence of transmission (Palmer et al., 1996; Buishi et al., 2005a). In 2009 the coproantigen prevalence in the mid-Wales zone remained at 8.8% (Mastin et al., 2011). In Datangma (Tibetan Sichuan) after 5 years of twice-annual dog dosing with PZQ, Echinococcus spp. coproELISA prevalence in

owned dogs had reduced from 50% to 17% (Yang *et al.*, 2009).

The more recent development of copro-PCR tests for detection of *E. granulosus* spp. DNA in faeces has shown great promise as a species-specific confirmatory tool for dog infection (Abbasi *et al.*, 2003; Stefanic *et al.*, 2004). PCR sensitivity for *Echinococcus* infection, however, is lower than coproantigen detection (Lahmar *et al.*, 2007; Boufana *et al.*, 2008). DNA detection may be best applied for confirmation of coproantigen tests, especially in the 'consolidation' phase of hydatid control, and where *E. granulosus* and *E. multilocularis* are co-endemic (Craig *et al.*, 2003).

#### E. granulosus reinfection in dogs

An important consideration for endemic canine echinococcosis in both baseline preintervention studies and for assessment of infection pressure in 'attack' and 'consolidation' phases of hydatid control, is to determine natural reinfection rates in dogs. Such information can be very useful in consideration of an optimized cost-effective dog dosing regimen, and to establish the time or period after cessation of dog-targeted control measures that canine echinococcosis reinfection may re-emerge. Despite this, relatively few epidemiological or control studies have assessed E. granulosus reinfection rates in dogs following a single deworming treatment, or after cessation of mass treatment. A single PZQ treatment of dogs should eliminate all E. granulosus worms to produce a 0% prevalence within 6 weeks post treatment (i.e. the pre-patent period). In theory, dogs should therefore be dosed every 6 weeks (i.e. approximately eight times per year) to prevent new infections establishing (WHO/OIE, 2001). In Rio Negro (Argentina), two cohorts of farm dogs (each >470 dogs) with an arecoline test baseline prevalence of around 40% exhibited reinfection prevalences of 0.8% and 3.5%, respectively, within 2 months after a single PZQ treatment, and by 8-9 months 10-21% of dogs were reinfected as determined by arecoline purgation (Larrieu *et al.*, 2000) (Table 12.3). Similarly, in Florida Department (Uruguay), a baseline arecoline prevalence for E. granulosus of 13.2% in 303 dogs had reduced to 0%

2 months after a single PZQ treatment, but rebounded to 5.4% at 3-4 months post treatment, and increased further to 18.6% at 8-9months (Cabrera *et al.*, 1996). Application of a  $4 \times 12$ -week PZQ dosing schedule in ~300 farm dogs in mid-Wales, with a baseline coproantigen prevalence of 8.8%, resulted in a reduction in coproantigen prevalence to 1.9%3-4 months later, and 0% at 12 months posttreatment. However, re-emergence occurred in Wales with a copro-prevalence of 1.7-9.6%over the following 12 months (A. Brouwer, W. Li, and P. Craig, unpublished) (Table 12.3).

These dog follow-up observations suggest that in some high or even moderate E. granulosus endemic areas, approximately 2–7% of owned farm dogs become reinfected by 3-4 months post PZQ treatment (without other control measures). Therefore, PZQ dosing frequencies should be implemented at least 4 times per year, and preferably 5-6 times per year (i.e. every 8-10 weeks) to reduce the possibility for dog reinfection. In the Chile Region XII hydatid control programme, dog dosing with PZQ was maintained at 8 times per year (i.e. every 6 weeks) for 7 years (1979–1986), then reduced to 2 times per year from 1987 to 1990 to save costs. However, dog prevalence (by the arecoline test) stayed at 1.6-5%, and ovine CE prevalence remained at 5–7%. Re-introduction of dog dosing with PZQ to 8 times per year (in 1991) was successful in Chile in reducing both ovine CE and

canine echinococcosis close to 0% by 3 years later (Gemmell, 1997).

### **Ovine hydatidosis**

The medium-term impact of CE control programmes is usefully measured by ovine CE prevalence at meat inspection in designated abattoirs/slaughterhouses. Other livestock such as goats, cattle, camels, and yaks may also be monitored, but the older age of slaughter of large ungulates reduces the short-term (1–5 years) use of these data. Sheep data should be collected at baseline and annually for three different age groups of sheep (lambs, juveniles, and adult sheep) for more sensitive variation in prevalence and cyst-intensity rates. Care should also be taken to differentiate CE from other lesions, such as those caused by Cysticercus tenuicollis (= Taenia hydatigena), especially in lambs (where cysts will be smaller and may therefore require histological or DNA confirmation) (Cabrera et al., 1995). Annual ovine CE prevalence data will enable the control authority to measure control impact and if necessary adjust dog dosing regimens, for example as applied in Chile Region XII (Vidal et al., 1994). Abattoir inspection of slaughtered sheep and other livestock also provides critical data for transfer from the 'attack' to the consolidation' phase of hydatid

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			Pv%		prevalence (%)				
Region (country)	Re	n	Day 0	Drug (x)	2	3–4	8–9	12	>12
Rio Negro (Argentina)	1.	476	42	PZQ(×1)	3.5	6.7	21.3		
		598			0.8	3.9	10.0		
Florida (Uruguay)	2.	303	13.2	PZQ(×1)	0	5.4	18.6	27.9	
Rio Grande (Brazil)	3.	44	7.7	PZQ	0	36.9			
				(several)	)				
Jendouba	4.	207	2.3	Arec	0	3.2	0	0	
Beja (Morocco)		168	4.9		6.5	3.6	6.3	16.7	
Turkana (Kenya)	5.	190	18	Arec		0		5	22
Shiqu (China)	6.	329	19.5*	PZQ(×1)	9.3*	2.2*		14.1*	
Mid-Wales (UK)	7.	609 [252–300]	9*	PZQ(×4)		1.9*	0.4*	0*	1.7–9.6*

Table 12.3. E. granulosus reinfection levels in dogs after treatment.

1. Larrieu *et al.*, 2000; 2. Cabrera *et al.*, 1996; 3. Farias *et al.*, 2004; 4. Lahmar *et al.*, 2007; 5. Wachira *et al.*, 1990; 6. Moss *et al.*, unpub. 2007–8; 7. Welsh Assembly Government, unpub. 2008–9. Arecoline test except CoAg. Arec = arecoline; PZQ = praziquantel; X = times dosed.

control. Trace-back of infected animals can be used to identify suspect farms/properties in order to impose restrictions on livestock and dog movement/treatment. The additional use of abattoir data for *T. hydatigena* infection in sheep can be useful in identifying potential transmission hotspots or breakdown in control (Economides and Christofi, 2002). In many endemic areas, however, most livestock slaughtering is done at home or in clandestine butchers, and therefore centralized abattoir data have limited use or are unobtainable.

Serodiagnosis of ovine CE is not sufficiently specific and sensitive to be of significant assistance in hydatid control programme surveillance (Craig *et al.*, 2003). However, if slaughterhouse data are unavailable or difficult to collect (e.g. in north-west Kenya), ultrasound scanning of sheep and goats can be assessed, though success has been limited (Njoroge *et al.*, 2000).

Use of sentinel livestock to detect natural exposure to E. granulosus has been successfully applied using lambs in hydatid control programmes in mid-Wales and Uruguay. In Wales, 6% of sentinel lambs became infected within 15 months from exposure in an area subject to full control (PZQ and education) over the previous 5 years (compared to 10%) in a neighbouring area with no intervention), indicating continued transmission from dogs to sheep (Lloyd et al., 1998). In Uruguay, one study to determine optimal PZQ dosing frequency found that sentinel lambs were not infected (0%) when a 6-weekly dog dosing regimen was used, but in contrast, 4-18% of sentinel lambs became infected when the dosing interval was extended to 12 or 16 weeks (Cabrera et al., 2002). Removal of old sheep (>5–10 years of age), which are the high-risk group for fertile hydatid cyst infection, may also be a control tool, if acceptable to the local population.

#### Human cystic echinococcosis/hydatidosis

The use of annual CE surgical/treatment incidence rate per 100,000 population for a hydatid control zone is the most frequently assessed parameter for public health impact.

Age-specific treatment incidence rates for the under-15 or under-10 years age groups can also provide data on recent transmission, as opposed to existing old CE cases (pre-intervention). Such data retrospectively indicated the positive impact of the Iceland educationfocused and the Chilean and Argentinian dog-dosing-based campaigns, or by contrast the failure of hydatid control in Sardinia. Such hospital derived data are, however, not always accurate, and health access may be poor for under-developed regions such as north-west Kenya and communities of the eastern Tibetan Plateau (Craig et al., 2003; Li et al., 2010). Active mass-screening surveys at community level using imaging techniques, especially portable ultrasound scanners, provide a more accurate approach for human surveillance in hydatid control programmes. Advantages of ultrasound scanning over hospital data include:

- the detection of asymptomatic cases;
- confirmation/clinical status of previous cases;
- early clinical information in respect of treatment options and natural history of disease;
- the true age-specific prevalence of abdominal CE;
- longitudinal data in follow-up; and
- an educational effect for rural communities (Macpherson *et al.*, 2003).

Ultrasound-based screening in CE endemic populations has been applied for surveillance in at least two hydatid control programmes: Rio Negro (Argentina) and Turkana (Kenya) (Macpherson and Wachira, 1997; Craig and Larrieu, 2006). In the Rio Negro programme, the ultrasound prevalence of CE in children (aged under 13 years) was shown to reduce from 5.5% to 1.1% over a 13-year period of intervention; furthermore, characteristic hydatid cyst pathology at ultrasound indicated that 65% of cysts were of the 'early growth' type (i.e. type CE 1) (Larrieu and Frider 2001; Frider *et al.*, 2001).

Serosurveys using sensitive and specific tests, such as antigen B-ELISA or immunoblot tests, have not been employed very extensively in surveillance of hydatid control programmes. Rather, use of hospital and/or ultrasound-based data sets were preferred because of their less equivocal diagnostic status. The DD5 agar test was, however, used to screen human sera for *Echinococcus* antibodies in the Falkland Islands, and was applied in the Rio Negro programme (later replaced by ELISA) to identify exposure in children. However, human serological testing alone without ultrasound remains controversial because of the tendency to create a list of seropositive cases (false positives) without clinical or image confirmation of CE (Rogan and Craig, 2002).

#### Other hydatid control measures and structures

#### Vaccines

Several hydatid control programmes have had poor impact, because of difficulties in maintaining the accepted standard of 6- or 12-week dog-dosing regimens for 5 years or more, and also to ensure that a sufficiently high proportion of dogs are treated. A recombinant oncosphere vaccine (EG95) against ovine echinococcosis has been developed (Lightowlers et al., 1996). Trials showed that two subcutaneous injections in sheep of the EG95 vaccine with Quil A adjuvant lead to production of antibodies that resulted in 96–100% protection against E. granulosus egg challenge infections for up to 12 months, and for up to 3 months in lambs born to vaccinated ewes (Lightowlers et al., 2003; Heath et al., 2003).

The EG95 vaccine provides the potential for implementation of a more rapid and cost-effective attack phase in parallel with dog dosing for hydatid control programmes. One effective strategy could be to combine spring and autumn vaccination of lambs/sheep with only twice-yearly PZQ dosing of dogs. Simulations of transmission in which hydatid control interventions were modelled (involving PZQ treatment of dogs, vaccination of sheep, and/or health education) indicated that vaccination of sheep alone could be highly effective if >90% of sheep are protected. More realistically, the models showed that a 75% vaccine cover of sheep, coupled with twice yearly dog dosing would have an equal effect (Torgerson and Heath, 2003). Undertaking definitive multicentric trials combining different EG95 vaccination regimens with or without dog deworming is strongly recommended by WHO (2011b).

Experimental recombinant adult worm vaccines against canine echinococcosis indicate possible effects on worm burden, worm development, and worm fecundity of E. granulosus (Zhang et al., 2006; Petavy et al., 2008). In experiments, however, dog numbers used were small and dogs were necropsied before patency at 26-45 days after challenge (with protoscoleces), so interpretation of vaccine efficacy was not robust (Torgerson, 2008). A functional dog vaccine against E. granulosus would provide a major intervention tool for hydatid control programmes, but significantly more research is required before this can be considered a viable option.

#### Education

In the absence of vertically directed measures (e.g. dog dosing), health education about the life cycle and transmission of E. granulosus could lead to a change in behaviour of dog and livestock owners, with resultant decrease in transmission. However, apart from the historically unique situation in Iceland in the 19th century (where for over 60 years or more the rural population changed its behaviour regarding home slaughter and dog contact), there is little direct evidence elsewhere of a marked effect of health education alone in reducing transmission of E. granulosus (Craig and Larrieu, 2006). Nevertheless, education is an important component of many successful hydatid control programmes, because it provides a route for community participation and ultimately acceptance of medium- to long-term vertical measures, particularly regular dog dosing, livestock husbandry measures, and annual surveillance. Education/training of slaughter personnel and veterinary technicians is therefore also important for successful implementation and data collection.

## Hydatid control administration and legislation

There have been three main administration models for hydatid control programmes:

**1.** A national or regional executive authority (Council or Commission, usually with government links), funded mainly by dog owners.

**2.** A direct government-funding authority, such as a Ministry of Agriculture or Health.

3. An NGO with funds from donor agencies.

Analysis of previously successful hydatid programmes indicates the need for specific legislation at regional or national level. Legislation needed includes:

- 1. effective meat inspection and disposal of offal;
- 2. prohibition of illegal slaughtering;

**3.** dog registration, testing, and treatment of infected owned dogs;

**4.** control of strays and elimination of owner-less dogs;

5. quarantine of premises with infected livestock; and

**6.** control of movements of food animals and dogs between infected and 'free' areas (Gemmell and Roberts, 1998; Craig and Larrieu, 2006).

Nearly 150 years of hydatid control programmes clearly shows that human CE can be eliminated as a public health problem. This is particularly so if a well-managed control authority (especially if led by a Ministry of Agriculture or Veterinary Services) implements a medium- to long-term (5-10 years) vertical campaign directed at treatment of owned rural dogs, with appropriate surveillance in sheep, dog, and human populations. Cooperation between veterinary and human health sectors is also important if public health indices and educational aspects are used effectively. Future programmes may be more efficient and costeffective than those previously implemented, if an integrated approach is used.

#### Conclusions

Since the first control activities for cystic echinococcosis took place in Iceland in the 1860s, the maintenance of eradication has been achieved there and reported for only two other island countries or territories (New Zealand and Tasmania). For continental regions, elimination or reduction of human CE as a public health problem is a more practical objective than parasite eradication or elimination in animal populations. Several hydatid control programmes have significantly reduced human CE incidence or prevalence rates, notably in Chile, Argentina, and Uruguay. In others, full or pilot hydatid schemes resulted in reduction in human CE cases, but significant incident rates remained or animal infections re-emerged after cessation of intervention measures (e.g. mid-Wales, Sardinia, northern Kenya, and north-west China).

Further research is needed in the 21st century to develop methods for reducing the 'attack phase' period and for achieving a permanent cost-effective 'consolidation' phase after dog-targeted hydatid interventions have ceased. Areas for improvement or development include:

- integrated assessment of vaccines for intermediate hosts with reduced dog-dosing frequencies;
- application of effective anti-hydatid anthelmintics for livestock (e.g. oxfendazole);
- development of diagnostic kits for rapid specific and sensitive on-site detection of dog infection;
- better livestock surveillance through lesion identification (e.g. DNA confirmation) at meat inspection, and by accurate ante-mortem serodiagnosis;
- development of an effective dog echinococcosis vaccine;
- use of cost-benefit models and control simulation outcomes together with coordination and integration with other relevant neglected zoonotic disease control programmes.

## **Canine Visceral Leishmaniasis Control**

#### Leishmania spp. and the leishmaniases

Leishmania are kinetoplastid protozoan parasites that are the causative agents of human and canine leishmaniases. The infection is transmitted from the blocked foregut of bloodsucking female sandflies. The infection process is facilitated by Leishmania-secreted proteophosphoglycans, which the sandflies regurgitate during feeding (Rogers et al., 2009). Many Leishmania spp. have been described, divided into two different subgenera: the Leishmania subgenus Leishmania, which occurs in both the Old World (OW) and the New World (NW), and the Leishmania subgenus Viannia, which is confined to the NW. The taxonomic framework for naming Leishmania spp. has been based on biological features such as the distribution of developmental stages in the sandfly vector, which separates Leishmania from Viannia, together with associated geographical and epidemiological data, especially the diverse clinical presentations of Leishmania infection (Lainson and Shaw, 1998; WHO, 2011a).

Human visceral leishmaniasis (VL) is caused by the two species of the Leishmania donovani complex, L. donovani and L. infantum, with two distinct epidemiologies (see below). Overtly symptomatic VL is generally considered to be fatal if not treated. However, many fully immunologically competent individuals exposed to L. donovani complex infections do not succumb to the disease, and some infections cause simple cutaneous lesions that do not visceralize. Nevertheless, human VL has been responsible for large, devastating epidemic outbreaks on the Indian subcontinent and in the Sudan. A common sequel of treated human VL, particularly on the Indian subcontinent, may be a disseminated cutaneous form, known as post-kala azar leishmaniasis (PKDL), which is considered to be highly infectious to the vector sandflies. In contrast, human cutaneous leishmaniasis (CL), caused by L. major, L. tropica or L. aethiopica in the OW, and the L. mexicana complex and the subgenus Viannia in the NW, may be less severe and self-curing, although occasionally L. aethiopica and L. amazonensis (the latter within the *L. mexicana* complex) give rise to diffuse cutaneous leishmaniasis (DCL). Notably, however, L. (V.) braziliensis of the Americas frequently metastasizes to cause severe mucocutaneous leishmaniasis (MCL), with disfiguring and potentially fatal destruction of the nasopharynx.

Most of these Leishmania infections are zoonoses, with important silvatic or peridomestic reservoir mammalian hosts that act as sources of infection to sandflies, which can then transfer Leishmania infection to humans. The taxonomy of Leishmania spp. has been largely confirmed by molecular methods such as multilocus sequence typing (MLST), except that several species have proved to be invalid synonyms, for example *L. chagasi*, which is a synonym of L. infantum and L. archibaldi, which is a synonym of L. donovani (Mauricio et al., 2000; Lukes et al., 2007; Quinnell and Courtenay, 2009). High-resolution molecular methods, such as multilocus microsatellite typing (MLMT), can reveal the population structure of individual species such as L. infantum, and track origins and migrations (Kuhls et al., 2011).

### The dog is the primary reservoir host of zoonotic VL

In the context of this chapter and this volume, the dog is the crucial primary reservoir host for VL due to *L. infantum* (but not for *L. donovani*). *L. infantum*-infected dogs may suffer fulminating fatal canine visceral leishmaniasis (canine VL) with both visceral and disseminated cutaneous infections. The dog is also a probable sporadic suburban reservoir host of CL/MCL due to *L. braziliensis*.

Criteria to incriminate the dog as a reservoir host of VL include:

- the abundance of dogs;
- their presence as a significant blood source for sandflies;
- their contact with sandflies;
- the prevalence of canine infection;
- the course of infection and accessibility of infection to sandflies; and
- carriage of the same parasite genotypes that are found in human infections (WHO, 1990, 2011a).

There is overwhelming evidence that the dog is the primary reservoir host for human VL due to *L. infantum*, as follows:

 Dogs are readily susceptible to infection with *L. infantum* (and both symptomatic and asymptomatic infections are common).

- Parasitaemias in dogs may be very high, particularly in the skin, and abundant amastigotes are thus accessible to sandflies.
- Infections in dogs may be prolonged for months or years, with sustained high parasitaemias.
- Dogs are fed on avidly by the same sandfly species that bite humans.
- Infected dogs are highly infectious to sandflies and this may be true even for asymptomatic dogs.
- Vector-borne human VL due to *L. infantum* is sympatric with canine VL (although canine VL is endemic in some regions where human cases of VL are rare or unknown, and more than 1000 cases are known of canine VL imported to non-endemic areas) (Paranhos-Silva *et al.*, 1996, Slappendel and Teske, 1999; Zaffaroni *et al.*, 1999).
- Strains of *L. infantum* with the same genotypes and phenotypes have been shown to occur sympatrically in dogs and humans, even when high resolution MLMT is used (Dereure *et al.*, 1999; Martin-Sanchez *et al.*, 1999, Kuhls *et al.*, 2011).
- Dogs have a close domestic and peridomestic association with humans.

Nevertheless, it has been difficult to prove unequivocally, for example by mapping acute cases of human VL and the distribution of dogs, that there is a directly significant correlation between dog ownership and the risk of human VL (Evans *et al.*, 1992; Cunha *et al.*, 1995; Costa *et al.*, 1999, Quinnell and Courtenay, 2009). This is not surprising as there are many potential confounding factors, such as:

- the focal abundance of sandfly vectors;
- the range of clinical presentation in dogs, from asymptomatic to fulminating infections, which may in part be dependent on the breed of the dog;
- the rapid turnover of dog populations and introduction of susceptible replacement puppies;
- the predominance of asymptomatic human infections;

- the role of age, nutritional status, and immune competence in susceptibility to human VL;
- the time lag between exposure to infection and appearance of symptoms;
- the mobility of humans, dogs, and the sandfly vector; and
- the varying degrees of exposure to sandfly bites due to behaviour of inhabitants.

In many regions where canine VL is endemic, individual dogs are valued highly as companions, as working or hunting animals, and for breeding. If owners have a comfortable socio-economic status, for example in some countries around the Mediterranean basin, they can devote considerable financial resources to their dogs. In such circumstances, the health of the dog, irrespective of the need to prevent sporadic human cases of VL, may be a primary impetus for interventions against canine VL. The dog may be given frequent and expensive veterinary examinations and treatments. Repetitive, non-curative therapies for canine VL may be applied, sustaining prolonged potential to infect sandflies, even though this might have long-term repercussions on the transmission dynamics of VL to the human population. However, in poorer regions, such as suburban slums in some regions of South America, prevalence of canine VL may be very high, affecting substantial populations of stray dogs and domestic dogs, and be undiagnosed and untreated.

From a wider perspective the overwhelming reason for the control of canine VL is its association with *L. infantum* and human VL. L. infantum and the zoonotic form of VL occur in more than 50 countries, encompassing southern Europe, North Africa, the eastern Mediterranean, China, and Central and South America. However, where L. donovani is the agent of human VL, in the Indian subcontinent, East Africa, and the south-western Arabian peninsula, the dog is not a primary reservoir host. Thus in India, the dog has no proven role and the disease is considered to be entirely an anthroponosis, in which cyclical epidemics are sustained by the reservoir of human infection, particularly PKDL, in conjunction with abundant sandflies and

new immunologically naïve generations of the human population. Further details of the geographical distributions of VL and CL, reservoir hosts, and vectors can be found elsewhere (Desjeux, 1991; WHO, 2011a). The incidence, severity, and global extent of the leishmaniases justifies the WHO selection of the leishmaniases as a major public health problem and one of its health priorities.

Despite the proven role of dogs as the primary reservoir host of L. infantum, transmission from human to human via the sandfly vector cannot be excluded. Studies on transmissibility of L. infantum (below) show that sandflies can occasionally be infected by feeding on humans with untreated symptomatic VL due to L. infantum (but this is far more likely if there is PKDL due to L. donovani). However, infection is rarely acquired when sandflies feed on immunocompetent humans with asymptomatic L. infantum infection. On the other hand, immunocompromised humans who are co-infected with HIV and L. infantum have been shown experimentally to be readily infectious to sandflies, and this could be an emerging source of infection if such untreated co-infections increase among vulnerable endemic communities.

Cats, rats, horses, and silvatic mammals such as foxes (*Cerdocyon thous*) and opossums (*Didelphis* spp.) in the New World, and foxes and jackals in the Old World, can carry *L. infantum* but infectiousness to sandflies appears to be low. While further research on such alternative mammal hosts may be of interest and they might rarely act as link hosts between transmission cycles, only the dog warrants the status of a primary reservoir host for VL due to *L. infantum* (Quinnell and Courtenay, 2009).

There is increasing evidence that the dog may also be an important host of *L. braziliensis*, the agent of human CL and MCL in Latin America. The establishment of canine *L. braziliensis* infections in periurban and urban areas may have led to outbreaks of human CL in Latin American cities. As a result, it has become relevant to consider common approaches to the control of canine leishmaniasis due *L. infantum* and *L. braziliensis* (Momen, 1995; Santos *et al.*, 1998; Reithinger and Davies, 1999).

## Research progress in the last decade

During the last 10 years there has been substantial research effort on *Leishmania* and the improvement of the control of leishmaniasis:

- The genomes of three *Leishmania* spp., *L. major*, *L. infantum*, and *L. braziliensis* have been sequenced, enhancing understanding of their comparative biologies, although as yet with little direct impact on control strategies for leishmaniasis (Peacock *et al.*, 2007). Multiple *L. donovani* genomes from Nepal have been sequenced in an effort to identify genetic determinants of drug resistance.
- Importantly, two new vaccines for canine VL have been produced and have shown some evidence of success in field trials. One (Canileish<sup>®</sup>, Virbac, Carros, France) has been licensed for use in Europe, revitalizing optimism that in due course a vaccine for human VL will be attained.
- A new oral drug, miltefosine, has been introduced for the treatment of human VL, although this is not appropriate for canine VL.
- Considerable progress has been made with combination drug treatments or modified single-drug chemotherapy schedules for human VL, although again not applicable to canine VL.
- New methods of reducing the contact between sandflies and dogs have been trialled, notably dog collars impregnated with pyrethroid insecticides and pouron pyrethroids, to kill and repel sandflies attacking dogs and thus impede the canine VL and human VL transmission cycles.
- A WHO technical report on control of leishmaniasis (WHO, 1990) has been updated (WHO, 2011a) and is essential reading for all those interested in the biology, epidemiology, and control of the leishmaniases. In the 1990s a workshop jointly sponsored by the Department for International Development (DFID, UK), the WHO, and the Pan American Health Organization (PAHO) produced a still helpful guide to the control of VL, including protocols for the treatment of

human cases, for serological and parasitological diagnosis, for insecticide spraying, and impregnation of bed nets (Arias *et al.*, 1996). Readers are also referred to two excellent recent reviews: Quinnell and Courtenay (2009), which provides some more details on aspects of zoonotic VL relevant to this chapter, and Romero and Boelaert (2010), which reviews control of zoonotic VL in Brazil.

#### **Control strategies**

For years, three fundamental strategies have been adopted for interventions against zoonotic VL, and remain the same, albeit with varying emphasis and some improvements. They are:

- Diagnosis and treatment of clinical cases either passively detected by referral of patients to public health workers and referral of dogs to veterinary surgeons, or actively detected by looking for cases in endemic communities.
- Culling of putatively infected dogs identified by clinical and, more usually, serological/parasitological surveillance of domestic and stray dog populations.
- Destruction of vector sandfly species by the residual insecticide spraying of dwellings, environmental fogging or, more recently, application of insecticides to dogs.

## Treatment: life-saving but not easy for human VL, unsatisfactory for canine VL

Early, accurate diagnosis and rapid treatment are fundamental to the control of zoonotic VL, because this saves the lives of human patients. In contrast, there is no reliably effective treatment for canine VL.

Anti-leishmanial chemotherapy for human VL may require supportive treatment for malnutrition, dehydration, or concomitant infection. Choice of drug may depend on the regional prevalence of drug resistance.

For 70 years the first-line anti-leishmanial drugs have been the pentavalent antimonials,

in the form of meglumine antimonate or sodium stibogluconate. Alternative drugs are amphotericin B deoxycholate, liposomal amphothericin B, pentamidine isothionate, or, more recently, aminosidine (paromomycin) or miltefosine. Treatment of human VL with antimonials is based on 20 mg/ kg for 28-30 days, intramuscularly or intravenously. Unfortunately, for anthroponotic VL (due to L. donovani) in India and Nepal, drug resistance to antimonials may reach 60%. Amphotericin B deoxycholate is given by intravenous infusion (0.75–1.0 mg/kg for 15-20 days). Liposomal amphotericin B recommendations vary, but it is given for much shorter periods and it may even be effective as two doses (total 20 mg/kg) or as a single dose (5mg/kg). Miltefosine requires 28 days (at approximately 2.5 mg/kg), and has the advantage of being an oral drug, although it is not appropriate for pregnant or potentially child-bearing women. Paromomycin sulphate is given for 21 days at 15–20 mg/ kg. Combination therapy can reduce treatment schedules, be a great advantage in treating epidemic outbreaks of human VL, and make emergence of drug resistance less likely. Pentavalent antimonials plus aminosidine, for example, can reduce treatment from 30 to 17 days. Other combinations include liposomal amphotericin B plus miltefosine; liposomal amphotericin B plus paromomycin; or miltefosine plus paromomycin. Amphotericin is considered the best option for VL in pregnancy and for treatment and maintenance chemotherapy in HIV-VL coinfection. Treatment of PKDL can be difficult and require longer courses. For zoonotic VL due to L. infantum, recommended treatments in order of preference are: liposomal amphotericin B (3-5mg/kg for 3-6 days up to a total of 21 mg/kg); pentavalent antimonials (20 mg/kg for 28 days); amphotericin B deoxvcholate (0.75–1.0 mg/kg daily or on alternate days, up to total of 2–3 g) (WHO, 2011a).

Pentavalent antimonials are much less effective for the treatment of dogs carrying *L. infantum*: such treatment may suppress parasitaemia and give clinical improvement, but not necessarily eliminate the organism or prevent relapse. The pharmacokinetic or other reasons for this are imprecisely known, but antimonials are rapidly excreted, and the abundance of dermal amastigotes in canine infections may be a factor. Nevertheless, in privileged circumstances dogs have been treated with antimonials and treatment may be used repeatedly to keep an animal alive. This practice carries a risk of generating new drug-resistant strains of L. infantum, which could spread among dog and human populations, so such repeated therapy with antimonials should not be given. Similarly, aminosidine treatment of dogs produces dramatic clinical improvement but rarely clinical cure: most dogs relapse 2-4 months after the end of therapy (Vexenat et al., 1998). A veterinary alternative is to treat canine VL with allopurinol as a leishmaniostatic but not a curative therapy (Lamothe, 1999). However, this requires prolonged maintenance treatment to avoid repeated relapse of infection and renewed infectivity for sandflies, again with the risk of propagating further canine and human VL. Thus, there is no satisfactory effective chemotherapy for canine VL. Development of new drugs for canine VL would seem to be of considerable veterinary research interest and empirical screening of large libraries may yield new leads.

## Diagnosis of canine VL: better rapid diagnostic field tests are needed

Reliable clinical signs of canine VL are not obvious until late in the disease. Late-stage signs include dermatological changes, emaciation, excessive claw growth (onychogryphosis), and lymph node enlargement (Ferrer, 1999). Furthermore, asymptomatic dogs may be highly infective to sandflies. In a veterinary clinic, parasitological examination (for example by microscopy of giemsa-stained sternal or lymph node aspirates) can be routine and helpful, but it is not practical or sufficiently sensitive for mass surveys.

Surveillance of dog populations to remove infected animals has thus depended on serological methods including mass surveys (Maia and Campino, 2008), usually with blood samples collected onto filter paper. Such surveys may be conveniently integrated with rabies control campaigns. Serological tests commonly use some form of ELISA or the indirect fluorescent antibody test (IFAT). Plate ELISAs are low-cost and may be established in-house rather than purchasing commercial assays: they require meticulous standardization with positive and negative controls, and external quality control. ELISA results are best read by optical density with a spectrophotometer, but positive and negatives can be recorded visually from the plate. Modified ELISAs include a dot-ELISA (Vercammen et al., 1998), which is performed on membranes instead of plates, and a FAST-ELISA, which uses whole blood as an adaptation for rapid field use (Babakhan et al., 2009). The IFAT requires a fluorescence microscope. A direct agglutination test (DAT) that is highly specific for human VL is also applicable to dogs if lower minimum positive titres are used. The DAT test depends on freshly prepared or lyophilized whole organisms as antigen, which is costly and difficult to obtain in quantity, and vulnerable to differences in reproducibility. The rK39 recombinant antigen dipstick provides a relatively low-cost commercially available rapid diagnostic test for serological diagnosis of VL in humans and animals. It gives an immediate result and can be used to make a rapid decision on intervention options when a dog is found to be positive.

The rK39 test functions less well in East Africa than Europe, but a modified format (rK28) has been developed in an attempt to improve sensitivity. Serological surveys have been adopted as a potential cornerstone of control campaigns for canine VL. The validity of serological screening and removal of seropositive dogs as a control strategy is discussed in more detail below.

# Culling dogs for control of VL: valid in principle, complex to implement

The ease with which canine VL is transmissible to sandflies is indisputable. In pioneering studies, Deane (1956) and Deane and Deane (1962) compared dogs and humans as a source of *L. infantum* infection to the principal vector in South America, *Lutzomyia*  longipalpis. Dermal amastigote infections were prolific in dogs but scanty in symptomatic, untreated human VL. Vasconcelos et al. (1993) confirmed the original observations of Deane and Deane (1962) that amastigotes could be recovered from symptomatic human VL. They isolated Leishmania from 7 of 18 patients by culture of skin biopsy samples. Some symptomatic human L. infantum infections, prior to treatment, may thus be infective to sandflies and propagate further human infections. However, it was much easier to infect sandflies by feeding them on the dogs than by feeding them on the human cases. No infections were acquired by Lu. longipalpis fed on treated human cases. Miles et al. (1999) confirmed the high transmissibility of canine VL to Lu. longipalpis by examining wild-caught sandflies. Up to 67% of engorged female sandflies collected from a kennel housing a dog with disseminated dermal VL were shown to be infected by dissection 5 and 7 days after collection. Infection rates in fed sandflies captured with a less discriminatory CDC light-trap, were much lower. This was not surprising, because as well as dogs, alternative hosts such as chickens or pigs were abundant in the endemic area. Similarly, xenodiagnosis experiments demonstrated that infection rates of 70-90% were common when sandflies were fed on symptomatic dogs, and overall infection rates were greater than 20% even when flies were fed on the normal skin of such animals. Furthermore, asymptomatic dogs can also be highly infective to sandflies (Molina et al., 1994; Vexenat, 1993, 1998; Miles et al., 1999; Quinnell and Courtenay, 2009). Thus, field and experimental observations indicate that the basic case reproduction ratio ( $R_0$ ) for canine VL is likely to be high in endemic areas, implying each case is likely to give rise to several new cases. The high  $R_0$  has been supported by careful population studies and mathematical models (Dye, 1992; Quinnell and Courtenay, 2009). Transmission among dogs and not involving sandflies, by sexual and congenital routes, is known to occur rarely, and not at levels adequate to sustain endemicity (Quinnell and Courtenay, 2009).

Unfortunately serological surveys for canine VL fail, partially because a proportion

of infected dogs are seronegative. Also, some seropositive dogs might be false positives or have self-cured and therefore not warrant destruction. Although the probability of demonstrating the presence of infection increases with serological titre (Quinnell and Courtenay, 2009), a proportion of serologically negative dogs are parasitologically positive, even though as many as three different serological tests are applied (IFAT, ELISA, DAT). Parasitology, although more sensitive than symptomology, is not as sensitive as serology, and parasitological tests may show less than 60% sensitivity. Furthermore, in a series of experimental dogs infected by sandfly bite, a proportion of the animals was able to transmit infection from early cutaneous lesions and in the absence of seroconversion (Vexenat, 1998; Miles et al., 1999). There are as yet no practical alternatives to serology that are more sensitive. Experimental trials with PCR (Roura et al., 1999) confirm that the sensitivity of serological tests is not optimal. By PCR, Ashford et al. (1995) detected infections in more than 30% of dogs that were apparently seronegative. There is evidence that both human and canine VL are controlled by the balance of cell-mediated (Th1) and humoral (Th2) immune responses. In humans, positive skin tests (Montenegro or leishmanin tests) are considered to be an indicator of cure but not of the presence of active infection. Thus skin tests are not likely to be an alternative diagnostic procedure for determining the presence of infection, but they might be useful for assessing exposure rates or cure rates in canine VL, as they are in human VL (Pinelli et al., 1994, 1999; Cardoso et al., 1998; Santos et al., 1998). This failure of serology to diagnose all infections is a severe constraint on the effectiveness of serological surveys as part of a control strategy. The limited sensitivity of serology indicates that the reduction in R<sub>0</sub> that is likely to be achieved by serological surveillance and culling of seropositive dogs will still allow endemic canine VL to be sustained. In addition, low examination rates, slow response times (Braga et al., 1998), compliance failures, and replacement of dogs with susceptible puppies are likely to prejudice the outcome of a serological survey and culling strategy.

Simple deterministic model considerations indicate the frailty of current serological screening and culling as the core of control campaigns against zoonotic VL. Thus, knowing fluctuating seroprevalence rates, estimates for serology coverage and failure rates, and the temporal aspect of surveys and the course of canine infection, it is apparent that current methods of serological surveillance and culling alone will still allow canine VL to be sustained and expand (Miles, unpublished observations), as clearly demonstrated by computer modelling of reduction and resurgence of prevalence by Courtenay *et al.* (2002).

In view of these various factors complicating implementation of culling it is not surprising that field trials, which may have inherent design weakness and multiple confounders, have had mixed and partially conflicting results (Nunes et al., 2008, 2010; Quinnell and Courtney, 2009; Romero and Boelaert, 2010). As indicated above, the future success of dog culling as a control strategy will depend on a highly sensitive rapid diagnostic test for field use (Maia and Campino, 2008) and immediate removal of infected dogs, which are not replaced by new susceptible animals, in combination with health education and strong community support. Furthermore, dog culling as a control strategy cannot ignore the immense importance and value that some communities may attach to their domestic and working dogs, with consequent understandable reluctance of such communities to accept full implementation of an optimal culling programme.

## Control of sandflies with insecticides: an essential element of VL control

Sandflies may be extremely abundant in endemic regions of canine VL. In the absence of resistance, sandflies are exquisitely sensitive to insecticides. DDT is effective, as are the synthetic pyrethroids (deltamethrin, permethrin, cypermethrin, and others), which have low toxicity and high residual activity. In localities where malaria and VL are sympatric, spraying against mosquito vectors of malaria can have a dramatic effect on abundance of sandflies and the prevalence of VL. Insecticides are used residually against sandflies, and applied to domestic and peridomestic resting sites. Occasionally, ultralow-volume spraying into the air (fogging) can help to stem epidemic outbreaks of VL. However, this blanket approach only reaches adult sandflies at the time of spraying. For long-term effect, ultra-low-volume spraying must be applied repeatedly, with high coverage of the affected area, and at seasonal peaks of sandfly abundance. Insecticideimpregnated bed nets offer protection against sandflies during sleeping periods at night. Barrier curtains treated with insecticides can restrict access of sandflies to houses. Topical insecticide treatment of dogs (below) may also reduce sandfly numbers.

# Comparative impact of treating human VL, culling dogs, and vector control

Few studies have attempted to assess the relative values of the treatment of clinical cases, the removal of infected dogs, and spraying against sandflies as components of a VL control campaign. Such studies are fraught with difficulty due to complexities of design, multiple potential confounders, and equivocal outputs.

Withholding treatment for overt clinical human VL, which is usually fatal if not treated, is clearly not an ethical option as part of comparisons of interventions. Comparative studies in which treatment of human VL is specifically withheld to assess its epidemiological impact are thus not available. Deane and Deane (1962) thought that outbreaks of human VL in Brazil depended on the abundance of the vector Lu. longipalpis, but believed that small sandfly populations could maintain endemic canine VL. Alencar (1961) assessed the impact of sandfly control with insecticides in a comparative study of interventions against human VL. With two groups of communities, he found that the incidence of human VL decreased only when insecticides were used in addition to the treatment of human cases and the removal

of seropositive dogs. This supported Deane and Deane's view of the significance of sandfly abundance and the importance of vector control. Studies of the impact of serological screening and removal of seropositive dogs are few and limited. The total removal of the dog population has been reported to be an effective control measure in China (Ashford, 1999). Ashford *et al.* (1998) were able to show a decrease in both the incidence of human VL and seropositivity rates in dogs when 69% of seropositive dogs were removed promptly by using the FAST-ELISA for serology. Failure of compliance did not allow removal of all the seropositive dogs.

Akhavan (1996) considered whether control of VL based on the three strategies of treatment of cases, culling of seropositive dogs, and spraying against sandflies, had been effective in north-eastern Brazil. He assumed that epidemics with increasing levels of incidence occurred every 10 years. The total cost of control campaigns was estimated at US\$95,000,000. It was further estimated that 68,000 DALYs had been gained, at a cost of US\$139 for each DALY recovered. The control campaign in northeastern Brazil has been difficult to sustain continuously. Nevertheless, Akhavan concluded that the campaign had been costeffective. It is not clear, however, what contribution to the campaign is attributable to the culling of seropositive dogs. More recent combination control trials in Brazil are summarized by Romero and Boelaert (2010): one trial showed reduction in incidence of human VL associated with a combination of insecticide spraying and dog culling (de Oliveira et al., 2003), one indicated a partial association (Costa et al., 2007), and a third showed a similar trend but was not significant (de Souza et al., cited in Romero and Boelaert, 2010).

## Vaccination and immunotherapy: some progress

The development of vaccines against human VL has been a research objective for decades, impelled by knowledge that introduction of

infective L. major to induce a lesion at a hidden cutaneous site (leishmanization) can protect against subsequent infection and potential facial disfigurement. Nevertheless, there are no attenuated, killed, or recombinant vaccines for human VL, although intensive research efforts continue. Two vaccines have been developed and commercialized for canine VL; their futures are dependent on conclusive demonstration of capacity to prevent severe clinical disease in dogs, and to stop transmission from vaccinated dogs that might acquire subclinical infections. In addition, it is essential that the serological response of vaccinated animals can be distinguished from that of dogs acquiring natural infection, because failure to separate them is a complication of effective surveillance. Leishmune® (Fort Dodge Animal Health, Brazil) is an FML- (fucose-mannose ligand antigenic fraction, of L. donovani) saponin vaccine for canine VL. In Brazilian field trials, the efficacy of Leishmune® was reported to be indicated by FML-seroconversion, skin test positivity, protection against clinical canine VL, blocking of transmission, and associated reduction of incidence of human VL in some but not all localities where vaccination was a supplementary intervention in control programmes (Borja-Cabrera et al., 2008; Palatnik-de-Sousa et al., 2009). Leishimmune® is also reported to have some immunotherapeutic potential (Borja-Cabrera et al., 2010) and the immunological response has been characterized in vitro (de Lima et al., 2010). FML-seroconversion did not cross-react significantly with standard ELISA for serological surveillance (de Amorim et al., 2010). Similarly, another candidate, prime boost vaccine DNA/ MVA, did not induce rK39 seroconversion (Carson et al., 2009). In a smaller field trial a L. infantum antigen with muramyldipeptide as adjuvant (LiESAp) was reported as having 92% efficacy, with 1/165 clinical cases in vaccinees versus 12/165 in controls (Lemesre et al., 2007). Several other second-generation vaccines are also under development, with varying degrees of success, including Leish-111f+MPL-SE vaccine which may have some immunotherapeutic potential (Trigo et al., 2010).
# Topical application of insecticides to dogs: a useful adjunct to control of VL

A promising approach to control of canine VL is to use pyrethroids in new ways, such as by dipping hosts or spotting-on insecticides to diminish sandfly attack and to kill biting sandflies (Xiong et al., 1995). Similar systems are effective against other insect vectors, for example in the form of ear tags on cattle. An emulsifiable concentrate of deltramethrin was effective for 5-6 months after application (Courtenay et al., 2009). One approach is the use of pyrethroid-impregnated protective bands for dogs, which slowly release insecticide that spreads over the host. Experimental trials have shown efficacy, and field trials have indicated potential to reduce incidence of canine VL. However, collars are vulnerable to shedding and can only be regarded as a supplementary adjunct to control programmes that deploy the principal means of diagnosis, surveillance, and more orthodox vector control (Killick-Kendrick et al., 1997; Killick-Kendrick 1999; Lucientes, 1999; Aoun et al., 2008; WHO, 2011a).

# Integration of disease control: not to be overlooked

Coordination of control activities across organizations responsible for human and veterinary health or the management of VL is imperative, and various models have been proposed (Arias et al., 1996; WHO, 2011a). Primary health care workers in the community, as well as veterinary surgeons, need to be able to recognize the clinical symptoms of canine VL and to know how to report the presence of canine VL through local health channels. Veterinary surgeons and zoonosis centres or similar organizations need to be equipped to make serological and parasitological diagnoses, and require clear guidelines on how to manage canine VL. Effective liaison between veterinary health authorities and human health authorities is essential, even if human VL has not yet been reported in the locality. This is because sporadic infant cases may go unrecognized, and be fatal. Informed

higher-level public health authorities will need to decide whether epidemiological survey for human and canine VL is justified, and if further cases are found whether to begin a coordinated and integrated control campaign. Where rabies surveillance and control campaigns are envisaged or in place, or where there are overlapping interventions against other insect vectors such as mosquitoes, it is essential to communicate across the control programmes and share resources whenever it makes logistic and economic sense.

# Health education and community support: fundamental to success

Health education and mobilization of community resources are fundamental but somewhat neglected areas of control of VL. Knowledge, attitude, and practices (KAP) studies are a useful means of understanding the extent of information on transmission and control of VL that are available to public health professionals, patients, and communities. There are often abundant and diverse levels of harnessing community support for control programmes, and increasing options for communication and health education such as radio, TV, computer, and mobile phone technologies which are dispersed to locations that previously had poor accessibility. Poor socioeconomic conditions associated with propagation of VL may not be altered easily, but other predisposing factors such as environmental degradation and chaotic husbandry of dogs and other domestic animals can be addressed (Marzochi et al., 2009). Community activities can include clinical surveillance and follow-up of treated patients, environmental surveillance, environmental improvement, and assistance with vector and reservoir control, and can be a driving force for behavioural change.

# Essential components of a control programme for zoonotic VL

 Efficient, rapid delivery of effective, lifesaving treatment for human VL, with zero cost to patients in poor communities, including coverage of ancillary costs of treatment such as secondary chemotherapy or travel to treatment centres.

- Serological surveillance of dog populations to detect the presence of canine VL as a predictor of human VL, and to encourage risk reduction and better management of domestic and stray dogs.
- Systematic enhancement of health education, communication, community support, and integration of activities by organizations with responsibilities for disease control.
- Environmental management and vector control to reduce breeding and abundance of sandflies, where possible implemented by community support.

For anthroponotic VL due to *L. donovani* (responsible for such large epidemic outbreaks on the Indian subcontinent and in the Sudan), case finding, diagnosis, treatment, health education, communication, and community support apply, but not the surveillance and management of dog populations. Among such impoverished, displaced, and highly vulnerable populations there will be limited capacity for community support, and an imperative need to improve nutritional status and to consider multiple complicating factors of such epidemic outbreaks.

## Conclusions

Treatment for canine VL is clearly unsatisfactory. The last-resort method in Europe of prolonged or lifelong allopurinol administration cannot be advocated for widespread use elsewhere, or as a control strategy, especially in view of the risk of sustaining endemicity. There is an urgent need for a cheap, highly effective drug for the treatment of canine VL. The drug should be simple to administer either orally or by few doses given by inoculation. There is a strong case for encouraging veterinary companies to take a research interest in this objective, with its concomitant impact on control of human VL. Clearly, better drugs for treatment of human VL are still desirable.

Epidemiological screening for *L. infantum*infected dogs should not be abandoned. Nevertheless, considerable improvements are essential if this method is to be effective. In particular, a reliable, specific, highly sensitive, rapid diagnostic test suitable for field use is essential. Such a test may be beyond reach, although new antigens and new formats are still being sought. Some thought could also be devoted to strategies for increasing dog examination rates and compliance with public health recommendations. Were a new treatment suitable for mass therapy to be found, this could virtually eliminate difficulties with compliance. Vaccination is a promising new development, remains a research priority, and requires further proof of efficacy in field trials. Incorporation of Leishmania antigens into the vaccine strain of rabies virus could be explored as a delivery system to provide simultaneous rabies and Leishmania vaccine coverage. In Europe, 50% of human L. infantum infections are associated with HIV coinfection (Alvar et al., 1996; WHO, 2011a), and most of these cases will receive prolonged antileishmanial therapy. In endemic areas in developing countries, some HIV/L. infantum coinfections in the community might provide a new reservoir of infection for sandflies, if not adequately treated, especially in areas where HIV and VL are increasingly sympatric. This may possibly shift the pattern of epidemiology of VL due to L. infantum to be less reliant on the dog as the primary reservoir host.

As described above, attention is repeatedly drawn to sandfly abundance as one of the most important factors in transmission of VL. Thousands of sandflies may be caught in a CDC trap during a single night: improved traps incorporating host or sandfly pheromone attractants are worthy of investigation as a method of reducing domestic sandfly infestations. Economic analysis, comparing cost of prevention against the financial loss due to disease, can provide a strong argument for control campaigns against leishmaniasis. A concerted effort is required to improve awareness of canine and human VL among communities and health professionals, and to give impetus to available and proven local and national strategies for control.

In launching control programmes, whether at community or national level, these should

not over-ambitiously involve all conceivable research dimensions of the problem and hypothetical cumbersome interventions, but be focused on the proven practical control methods to interrupt transmission and disease, which are implementable as a simple, manageable, and cost-effective package, supported and sustained by communities.

#### **Final Conclusion**

Rabies, echinococcosis, and leishmaniasis still represent a significant public health problem in most endemic areas. In some of them, they are increasingly reported and this is a cause of major concern for the future, if no comprehensive control programmes are initiated soon. Progress has, however, been achieved during the past 10 years in the prevention and control of these major canine zoonotic diseases.

In the field of rabies, a change of paradigm for human rabies prevention through the control and elimination of rabies in dogs has been promoted by international organizations since 2005. The Gates Foundation decided in 2008 to support this approach with a grant of US\$10 million. This funding is currently being used to implement pilot projects in three developing countries which should, by early 2014, have demonstrated the feasibility of the paradigm shift and its costeffectiveness. Today, many more countries in Africa and Asia are considering tackling their human and dog rabies problem than at the end of the 20th century. Rabies is the first neglected zoonotic disease to be targeted for elimination at the regional level: all Latin American countries are committed to eliminate human dog-mediated rabies and stop dog-to-dog transmission by the year 2015. The ten countries of the ASEAN (Association of South East Asian Nations) together with China, Japan, and the Republic of South Korea and the other rabies-endemic countries that are part of the South East Asian Region of WHO, such as Bhutan, India, Nepal, and Sri Lanka, have endorsed a strategy towards the elimination of rabies by the year 2020.

In the field of leishmaniasis, during the past 10 years new vaccines against canine VL

have been developed and used in field trials with the first results published in 2008–2010. The use of insecticide-impregnated dog collars is considered a promising approach with the potential to reduce the incidence of canine VL. The final demonstration of the impact of those new tools on canine VL occurrence and transmission in mass campaigns is still missing, but definitive trials should be conducted soon.

In cystic echinococcosis, alternative strategies involving vaccination of sheep with the recombinant oncosphere vaccine EG95, in addition to classical interventions, are expected to have a much higher chance of success in affected countries. Towards this goal, controlled trials using EG95 aiming at definitively demonstrating the added value of sheep immunization with or without dog deworming to control and eliminate the disease in humans and animals, will be initiated very soon.

Gaining access to dogs remains the major factor for success or failure of control programmes for zoonoses in which dogs play a pivotal role. The full collaboration of dog owners is very difficult to obtain, especially when coercive measures have to be taken, or when dog handling entails some risks or requires considerable efforts from the owner. This is compounded by reports indicating that unsupervised or insufficiently supervised dog populations are increasing in most developing countries, particularly near urban centres, due to the increasing availability of food sources. Dog removal is not the solution, as it does not have a sustainable impact on dog population size and is unacceptable to and/ or counterproductive in many local communities. Comprehensive dog population management guidelines have been developed during the past 3 years by international governmental organizations and NGOs, and should be consulted by national governments and/or the civil society to develop policies based on best practices and animal welfare standards.

Effective control of these diseases, whether canine or human, demands political will, recognition of cost benefits, coordination, and integration with other relevant disease control programmes and an investment from the countries themselves and the international community. The impact on health and the economy of these neglected zoonotic diseases is now better recognized at the national and international levels. However, as the share of international global assistance for health devoted to the control of neglected zoonotic diseases (NZDs) has traditionally been very small, the subject area may remain under financial constraints unless new funding sources and mechanisms are identified. This issue has been addressed by the WHO/FAO/OIE interagency meeting on planning NZDs prevention and control held in June 2011 in WHO Headquarters. These three organizations have agreed to look together for resources to invest in a minimum 'Priority NZDs Portofolio' which includes dog rabies and cystic echinococcosis (WHO, 2011b).

# Note

<sup>1</sup> www.wspa-international.org/latestnews/2010/bali\_rabies\_vaccination.aspx, accessed 20 June 2012.

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# **13** Fertility Control in Dogs

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Fertility control is used as a broad term for both contraception, that prevents the birth of offspring but maintains the potential for fertility, and sterilization, that renders animals infertile (Munson, 2006; Kutzler and Wood, 2006). Fertility control can be achieved through surgical sterilization or via chemical sterilization and contraception. Compared to surgical sterilization, chemical contraception is safer and less expensive, as it does not involve anaesthesia, welfare risks associated with surgery, and costs of specialized staff and facilities (Kutzler and Wood, 2006; Schmidt et al., 2009; Cathey and Memon, 2010). Chemical contraception is also more efficient than surgical sterilization, as many more animals can be treated with a contraceptive compared to numbers that can be neutered or spayed per unit time (Massei et al., 2010; Levy, 2011).

In recent years, the potential market for contraceptives and a growing public interest in alternatives to surgical sterilization for companion animals, wildlife, and livestock have fostered investments and research into the development of novel fertility control agents (Naz *et al.*, 2005).

Contraceptives are thus increasingly used for mitigation of human–wildlife conflicts and for wildlife disease management (Fagerstone *et al.*, 2010; McLaughlin and Aitken, 2011), and as alternatives to surgical sterilization in livestock and zoo animals.

In companion animals, contraceptives are used for preventing reproduction, suppressing male sexual behaviour such as spraying, roaming, and aggressiveness, treating prostatic hyperplasia, and reducing risks of mammary tumours (ACC&D, 2010; Goericke-Pesch et al., 2010). In wildlife, the use of contraceptives is advocated for conflicts exacerbated by overabundant animal populations and traditionally tackled by lethal control. Origins of these conflicts involve disease transmission, crop and forestry destruction, traffic accidents, predation on livestock and game species, and attacks on humans. Community opposition to the use of mass culling to manage these conflicts is widespread because of questions over its humaneness and potential environmental impact when large number of carcasses have to be buried, or when poisoning is used. This growing public antipathy towards lethal methods places increasing constraints on options for population management, particularly for high-profile animal species such as dogs, cats, monkeys, and elephants. As a result, fertility control is increasingly advocated as a safe, humane, and effective means for resolving human-wildlife and human-companion animals (particularly dog) conflicts, especially when culling is unacceptable, unfeasible, illegal, or unsustainable.

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# Fertility Control to Reduce Disease Transmission

Fertility control has been advocated as a means to reduce contact rate and disease transmission between individuals in the context of activities for the control of wildlife diseases and zoonoses. Several theoretical and field studies have been carried out to determine the impact of fertility control on zoonoses in wildlife and in free-roaming cats and dogs. Examples for zoonoses such as bovine tuberculosis, brucellosis, leptospirosis, and rabies are provided in Table 13.1. Many studies indicated that culling can lead to immigration, social disruption, and actually result in increased contact rate as animals tend to move over long distances to fill the voids left by those that have been removed from the population, and to re-establish territories (e.g. Bolzoni et al., 2007; Woodroffe et al., 2009). Conversely, fertility control is less likely to affect social organization, as animal movements in particular are less affected by reproductive inhibition than by culling (e.g. Swinton et al., 1997; Tuyttens and MacDonald, 1998, Saunders et al., 2002). Contraception also offers an added benefit, as the elimination of reproductive behaviour results in a decreased contact rate between animals, and thus in a lower risk of disease transmission (Killian et al., 2007; Ramsey, 2007).

The renewed interest in contraceptives to manage wildlife is also based on field and theoretical evidence suggesting that an effective, economically sustainable reduction of free-roaming animals can only be achieved by chemical sterilization, particularly in areas where veterinary care is not widely available nor affordable (Levy, 2011). The inability to sterilize a high proportion of free-roaming dogs through surgical sterilization was quoted as the main factor responsible for the failure of the Animal Birth Control (ABC) in India (Menezes, 2008). On the other hand, an intensive 8-year ABC in Jaipur (India), carried out on 24,986 dogs, resulted in sterilization of 64% of the females and in a decrease in rabies incidence (Reece and Chawla, 2006). In another Indian town, Jodhpur, a 3-year ABC programme led to 62-86% of free-roaming female and male dogs sterilized (Totton et al.,

2010). Although these studies demonstrated that well-coordinated surgical sterilization can decrease the number of dogs, such programmes are likely to be significantly more expensive than those based on catch-injectand-release where dogs are caught, injected with a rabies vaccine and a contraceptive, and immediately released (Massei et al., 2010). Dog owners may be reluctant to consider surgery for other reasons than just cost. A study in Sao Paulo, Brazil, found that 56.5% of people who had adopted shelter dogs were against surgical sterilization, quoting compassion (58.1%), unnecessary procedure (11.4%), cost (9.5%), and behavioural changes (4.8%) as reasons against this method (Soto *et al.*, 2005). Similarly, on Isabela Island (Galapagos), dog owners more frequently selected chemical castration over surgical castration to retain their dogs' perceived protective and hunting behaviour, and to avoid anaesthesia (Levy et al., 2008).

Recently developed mathematical models suggest that using contraceptives in conjunction with rabies vaccination considerably decreased the effort required for rabies elimination, by reducing both the proportion of dogs to be vaccinated against rabies and the time to achieve rabies elimination (Carrol et al., 2010). These findings confirm the predictions of previous models indicating that adding fertility control to vaccination could be more efficient than simple vaccination in eliminating diseases such as rabies in foxes, leptospirosis in brushtail possums, and tuberculosis in European badgers (e.g. White et al., 1997; Smith and Cheeseman, 2002; Ramsey, 2007) (Table 13.1).

# Animal Reproduction and Potential Targets for Fertility Inhibitors

Contraception can be achieved by preventing gamete formation, conception or implantation, or by disrupting pregnancy and causing resorption or abortion.

The cascade of hormones leading to reproduction is regulated by the gonadotropin-releasing hormone (GnRH), which is produced in the hypothalamus at the base

Species	Aim	Method	Conclusions	Ref.
Fox <i>Vulpes vulpes</i>	Evaluate impact of culling, fertility control and rabies vaccination for rabies control	Model	Integrating fertility control with rabies vaccination is more successful than rabies vaccination only	1
European badger <i>Meles meles</i>	Test fertility control to eliminate bovine tuberculosis	Model	Fertility control integrated with culling can eliminate the disease	2
Bison Bison bison	Evaluate immunocontraception to decrease transmission of brucellosis	Field trial	The use of single-dose immunocontraceptives is suggested to avoid disease vertical transmission	3
Possum Trichosurus vulpecula	Test effects of fertility control on possum behaviour and leptospirosis transmission	Field trial	Fertility control does not affect social organization but reduces disease transmission due to decreased contact rate	4
Dog <i>Canis familiaris</i>	Test fertility control to improve efficiency of rabies elimination in urban dogs	Model	Fertility control added to rabies vaccination reduces the proportion of dogs to be treated and the duration of vaccination campaigns	5
Dog <i>Canis familiaris</i>	Evaluate the effect of surgical sterilization on population size in the context of rabies control	Field trial and model	Sustained surgical sterilization can reduce population size and in the long term lead to rabies elimination	6

Table 13.1. Examples of empirical and theoretical applications of fertility control to control/eliminate zoonoses in wildlife and dog populations.

References: 1. Smith and Wilkinson, 2003; 2. White et al., 1997; 3. Miller et al., 2004; 4. Ramsey, 2007; 5. Carroll et al., 2010; 6. Totton et al., 2010.

of the brain. GnRH controls the release of the pituitary gonadotropins LH (luteinizing hormone) and FSH (follicle-stimulating hormone). These gonadotropins regulate steroid hormones that drive sperm production, follicular development, and ovulation. In females, FSH stimulation of the follicles in the ovary results in secretion of oestrogen which in turn promotes the development of female secondary sexual characteristics, such as breasts, induces oestrus behaviour, vulvar swelling, and regulates vaginal secretions. When oestrogen production reaches a threshold, a surge of GnRH and LH is followed by ovulation. After ovulation, the production of oestrogen decreases; FSH and LH cause the remaining parts of the follicle to transform

into the corpus luteum which produces significant amounts of hormones, particularly progesterone and to a lesser extent oestrogen. Progesterone is produced by both the corpora lutea and the placenta and is critical to support pregnancy.

In males, FSH is responsible for the initiation of spermatogenesis at puberty, and at the beginning of each reproductive season for those species that are not sexually active all year round. LH causes the testes to produce testosterone which stimulates and maintains spermatogenesis. Testosterone plays a key role in the development of male reproductive tissues, such as the testis and prostate, and in promoting secondary sexual characteristics such as manes in lions, ornamental feathers or bright coloration in birds, and antlers in deer. Testosterone is also responsible for aggression, courtship, and mating.

Feedback mechanisms between GnRH and gonadotropins ensure that the production of these hormones is increased or reduced to promote and maintain reproduction. Therefore, suppression of GnRH or of FSH and LH interferes with ovulation, spermatogenesis, gamete transport, embryo implantation, and maintenance of pregnancy.

The reproductive cycle and gametogenesis can thus be disrupted by administration of substances that interfere with the synthesis or release of hormones produced by the hypothalamus, the pituitary gland, or the gonads. In males, chemical sterilization can also be achieved by some chemicals inducing testicular sclerosis and permanent sterility. In females, another target for contraceptives is the zona pellucida (ZP), a group of proteins that surrounds the ovulated egg and allows species-specific sperm recognition and fertilization.

#### Fertility inhibitors for dogs

The following section presents a brief review of fertility control agents commercially available or widely tested on several species, with particular focus on those used in free-living carnivores, zoo carnivores, and companion animals such as cats and dogs. Taking into account potential field applications for freeroaming dogs, the review included only those agents described as effective to induce infertility for at least 6–12 months after one or two doses. Some examples of contraceptives that are very effective in fully controlled companion animals, but that cannot be regarded as suitable for free-roaming dogs are provided.

Unless specific references are quoted, most of the information on zoo animal contraceptives was derived from the Association of Zoos & Aquariums (AZA) Wildlife Contraception Center at the St Louis Zoo,<sup>1</sup> and information on contraceptives for dogs and cats from the Alliance for Contraception in Cats and Dogs.<sup>2</sup>

## Steroid hormones

Steroid hormones such as progestins, oestrogens, and various combinations of oestrogens and progestins are frequently used as reproductive inhibitors in zoo species and in some wildlife species. The proposed mechanism of action of steroid hormones includes interference with folliculogenesis, ovulation, and egg implantation in females, and impairment of spermatogenesis in males. Higher doses are required to block ovulation than to achieve contraception: therefore it is possible that ovulation, physical, and behavioural signs of oestrus occur in animals that are otherwise effectively contracepted (Brache *et al.*, 1990).

Synthetic progestins are available in a variety of formulations and include megestrol acetate (MA), melengestrol acetate (MGA), levonorgestrel, and norgestrel.

MA, used for dogs and cats over several decades in many countries under different brand names, was found to postpone oestrus in 92% of female dogs provided that it was administered orally for 8 days starting at a very specific time of the oestrus cycle (proestrus). The requirement for multiple, specific doses at a very precise time of a dog's cycle makes this agent a classic example of a contraceptive that is very effective in confined companion animals but unsuitable for field applications to free-roaming dogs.

Synthetic progestins are not recommended in pregnant animals because they might induce stillbirth or abortion in some species, or they might affect parturition by suppressing uterine contractions (Asa and Porton, 2005). Some progestins, such as MGA, have been widely used in zoo animals and are highly effective on many carnivore species, primates, and ungulates. In these species, an MGA implant can induce infertility for at least 2 years or longer, depending on species. However, MGA is associated with a variety of uterine pathologies and its use is not generally recommended for long-term contraception of canids and felids (Munson, 2006; Moresco *et al.*, 2009).

#### Gonadotropin-releasing hormone agonists

GnRH agonists are proteins that mimic GnRH and stimulate production and release

of FSH and LH. Agonists do not quickly dissociate from the GnRH receptors and their administration initially causes oestrus and ovulation (the 'flare up' effect), followed by prolonged ovarian quiescence (Gobello, 2007). The activation of the reproductive system also results in temporary enhancement of testosterone and semen production in males; females treated with a GnRH agonist should be considered fertile for 3 weeks following administration of an implant containing a GnRH agonist.

The effectiveness of GnRH agonists depends on a variety of factors including the agonist potency, the release system, the dose rate, and the duration of treatment (Gobello, 2007). The side effects of GnRH agonists are generally similar to those associated with removal of the gonads but are reversed once the treatment, often administered through an implant, is suspended; however, GnRH agonists should not be used during pregnancy, as they may cause abortion (Asa and Porton, 2005).

GnRH agonists, Among deslorelin (Suprelorin<sup>™</sup>, Virbac, Carros Cedex, France) available as implants can induce a 1-2 year contraception in cats and other felids, wild dogs, and in tammar wallabies (Macropus eugenii) (Munson et al., 2001; Bertschinger et al., 2002; Herbert and Trigg, 2005; Munson, 2006).When tested on dogs, deslorelin postponed oestrus in females for periods of up to 27 months (Trigg et al., 2001). Suppression of reproductive function in male dogs was doserelated: spermatogenesis was suppressed for more than a year in 14 of 16 dogs administered deslorelin, and treatment-induced effects on fertility were reversible in both sexes (Trigg et al., 2001).

The GnRH agonist, azagly-nafarelin (Gonazon<sup>™</sup>, currently not produced, but formerly manufactured by Intervet International B.V., Boxmeer, The Netherlands), administered as implant, was found to provide at least 1-year reversible contraception for female dogs. In a follow-up trial, female dogs were administered a second implant left in place for 18 months. This second dose prevented oestrus in 92% of the animals. Gonazon<sup>™</sup> was also successful in preventing puberty in young bitches for at least one year and in suppressing oestrus in female cats for at least 24 months with no other side effects observed (Driancourt *et al.*, 2006; Rubion *et al.*, 2006). A study on male dogs showed that Gonazon<sup>TM</sup> implants induced a 96% decrease in testosterone concentration for at least 6 months in 81% of the animals tested. Concurrent reduction of aggressive behaviour was recorded in 62% of dogs older than 6 years and in 73% of dogs younger than 3 years of age (Goericke-Pesch *et al.*, 2010).

#### Immunocontraceptives

Immunocontraceptive vaccines act by inducing antibodies against proteins or hormones essential for reproduction and thus causing infertility. Immunocontraceptives such as gonadotropin-releasing hormone (GnRH) vaccines inhibit gamete production by preventing ovulation and spermatogenesis. Zona pellucida (ZP)-based vaccines inhibit gamete function and conception. The zona pellucida is a layer of proteins that surrounds the egg and allows egg–sperm binding and fertilization. The ZP is among the most widely studied target for immunocontraceptive vaccines (Gupta and Bansal, 2010).

The effectiveness, longevity, and side effects of immunocontraceptive vaccines depend on many factors that include sex, age, and species as well as active ingredients, formulation, and dose of the vaccine and of the adjuvant (Miller *et al.*, 2008; McLaughlin and Aitken, 2011).

ZP immunocontraceptive vaccines have been used successfully to prevent fertilization in wallaby, mice, horses, white-tailed deer, monkeys, seals, elephants, bears, kangaroos, and possums (McLaughlin and Aitken 2011; Kirkpatrick et al., 2011). Among the most successful, a ZP vaccine called SpayVac<sup>™</sup> (ImmunoVaccine Technologies, Halifax, Nova Scotia, Canada), administered as a single injection, has been effective in white-tailed deer and horses for up to 4 years (Fraker *et al.*, 2002; Killian et al., 2004, 2008). In dogs and cats, early trials with ZP-based vaccines were promising but later studies showed no reduction in fertility (Levy, 2011). Contradictory findings between studies might be due to differences in the source and method of

preparation of ZP, vaccine formulation, type of adjuvant used, and differences in vaccination schedule (Levy, 2011; J.F. Kirkpatrick, pers. comm.). As ZP-based vaccines prevent fertilization but do not affect ovulation, treated animals still exhibit oestrus, and in some species these individuals have more oestrus cycles than controls (Miller *et al.*, 2000; Nuñez *et al.*, 2010). This would be a disadvantage for disease control in free-roaming dogs, as females in oestrus would still attract males and thus increase contact rate between animals.

GnRH-based immunocontraceptive vaccines stimulate the production of antibodies that bind to naturally occurring GnRH, and thus prevent the release of both LH and FSH. Without these two hormones in the bloodstream, the vaccinated animal does not reproduce. Several GnRH-based immunocontraceptive vaccines have been developed and tested on many species of mammals, including humans. The majority of these vaccines have been designed for applications in livestock and companion animals that can be treated with multiple doses (Naz et al., 2005; McLaughlin and Aitken, 2011). However, single-dose GnRH-based vaccines, specifically developed for wildlife, appear promising for potential use in free-roaming dogs. One GnRH vaccine that has seen rapid developments over recent years is Gonacon<sup>™</sup>, currently registered in the United States as a contraceptive for whitetailed deer. Gonacon<sup>™</sup> consists of a synthetic GnRH coupled with a mollusc protein and an adjuvant called AdjuVac<sup>™</sup> (National Wildlife Research Center, Fort Collins, Colorado), the latter based on a modified version of Johne's disease vaccine. Formulated as an injectable, single-shot vaccine, Gonacon<sup>™</sup> induces infertility for several years after administration of a single dose. Gonacon<sup>™</sup> has been shown to cause infertility in deer, wild boar, pigs, cats, dogs, horses, bison, and ground squirrels for at least 1-4 years after a single injection (e.g. Miller et al., 2000; Killian et al., 2008; Massei et al., 2008, 2012; Gray et al., 2010). As Gonacon<sup>™</sup> prevents ovulation, treated females do not exhibit oestrus behaviour.

In most animals, vaccination with Gonacon<sup>™</sup> does not affect behaviour or physiology but in some species a granuloma (i.e. thickened tissue filled with fluid) may appear

at the injection site. In cats, 93% of females treated with a single injection of Gonacon<sup>™</sup> remained infertile for the 1st year following vaccination, whereas 73, 53, and 40% were infertile for 2, 3, and 4 years, respectively (Levy et al., 2011). Two years after vaccination, 6/20 cats had a palpable, non-painful injection site granuloma. Dogs treated with Gonacon<sup>™</sup> showed adverse injection site reactions relatively soon after injection, with formation of sterile abscesses and draining tracts at the injection site (Levy, 2009). Following these findings, a new formulation of Gonacon™ was produced with the intent of minimizing injection site reaction in dogs while maintaining long-term efficacy. Pilot trials have just started to test this new formulation (L.A. Miller, pers. comm.). In parallel, Bender *et al*. (2009) demonstrated that Gonacon<sup>™</sup>, administered in conjunction with a rabies vaccine, did not affect parenteral rabies immunization in female dogs. Further progress has also been achieved in the development of combined vaccines for rabies and immunocontraception. Wu et al. (2009) inserted the coding sequence of GnRH into the glycoprotein gene of the rabies virus ERA strain, and showed that the recombinant rabies-GnRH virus induced antibodies against GnRH in treated mice, and protected 100% of the animals after rabies virus challenge. This suggested that combined rabies and GnRH vaccines may have potential for both dog rabies and dog population control, although the effect and long-term efficacy on reproduction remain to be tested in this species.

A wide spectrum of technologies, ranging from recombinant vaccines to fusion proteins has been used in various animal species to develop novel immunocontraceptive vaccines that could ultimately also be tested on dogs. For instance, recombinant GnRH-based vaccines have been successful in inducing infertility in male and female cats for at least 20 months after administration of two doses (at 0 and 28 days), with no evidence of tissue or organ damage (Robbins et al., 2004), and recombinant GnRH fusion proteins, used in three doses, rendered 92% of heifers sterile for at least 6 months (Geary et al., 2006). In dogs, many compounds aimed at non-surgical contraception are being explored: these include

targeted delivery of cytotoxins for chemosterilization, silencing genes that control reproduction, and phage-peptide constructs for immunocontraception (ACC&D, 2010).

## Chemosterilants

Chemical castration in male dogs can be induced by injecting particular chemicals into the testes, epididymis, or vas deferens to cause lack of sperm in semen and thus infertility.

Zinc gluconate neutralized by arginine has been used since 2003, under several commercial brand names, as a permanent chemosterilant in male dogs. When administered by direct injection into the testicles, this chemical causes sclerosis of the testes and sterility. Zinc gluconate-based Neutersol™ (Addison Biological Laboratory Inc., Fayette, Missouri) was approved in the United States by the Food and Drug Authority for chemical sterilization of male puppies. Neutersol<sup>™</sup> produced successful chemical sterilization in 99.6% of the 223 male puppies aged 3-10 months. Neutersol<sup>™</sup> does not require the use of general anaesthesia, though sedation is recommended to prevent movements of the dog during injection. Correct injection technique was found critical for the safe use of Neutersol<sup>™</sup>, that was otherwise associated with ulceration of the scrotum and painful swelling of the testes. Unlike surgical castration, Neutersol<sup>™</sup> can sterilize dogs without removal of the testicles so that testosterone is not completely eliminated (Kutzler and Wood, 2006). Levy et al. (2008) found that injection-site reactions occurred in 3.9% of the 103 dogs treated with zinc gluconate, and that basal testosterone concentration in treated dogs decreased but was similar to untreated dogs 2 years after treatment. Thus, secondary male characteristics such as roaming, marking, aggression, or mounting may be displayed.

Zinc gluconate is currently available in Mexico, Colombia, and Bolivia as Esterilsol<sup>™</sup> (Ark Sciences, New York, New York) and in Brazil as Infertile<sup>™</sup> (Rhobifarma Indústria Farmacêutica, Hortolândia, Brazil). A study conducted in Mexico, found that this compound induced absence of sperm or semen in 52 out of the 53 dogs administered a single dose per testis; ulcers related to poor injection technique occurred at the injection side in 2.6% of the dogs. However, the incidence of ulcers decreased as veterinarians started using separate needles for each injection (Esquivel LaCroix, 2006).

The low cost, ease of use, and cultural acceptance of a sterilization method that does not require removal of the testes make zinc gluconate a valuable tool for large-scale sterilization campaigns, particularly in areas lacking clinical facilities or skilled staff (Kutzler and Wood, 2006; Levy *et al.*, 2008; Soto *et al.*, 2009).

# Conclusions

A fertility control agent suitable for controlling population size of free-roaming dogs should have the following characteristics:

1. no unacceptable side effects on an animal's physiology, welfare, and behaviour;

be effective when administered in one dose;
 render all or the majority of animals infertile for one or more years;

**4.** prevent female reproduction, and ideally inhibit reproduction in both sexes;

5. be safe when administered at any time of the reproductive cycle or to pregnant animals;

**6.** have no effect on or be affected by other drugs, such as vaccines, used to control diseases;

**7.** be relatively inexpensive to produce and to deliver;

**8.** be available as an injectable, implant, or oral formulation;

9. be species-specific;

**10.** be stable under a wide range of field conditions.

Of the several fertility control agents currently available for companion and zoo animals, very few meet most of these requirements. For instance, many contraceptives are too expensive to be used in large-scale programmes, no single-dose oral contraceptive can induce infertility for 1 year, several compounds must be administered at specific times of the cycle to maximize effectiveness, and should not be given during pregnancy. For dogs that are fully confined or can be made accessible through their owners upon request, repeated dosing with contraceptives is feasible but likely to be expensive, particularly in developing countries.

However, novel contraceptives recently formulated for wildlife species, and in some instances specifically developed for dogs, could be used as practical, feasible alternatives to surgical sterilization for large-scale sterilization of free-roaming dogs. For instance, in rabies elimination campaigns where dogs are caught and injected with rabies vaccines, the same animals could receive a dual treatment (vaccination plus fertility control) and be released immediately (Massei, 2008; Bender *et al.*, 2009) provided the fertility control treatment has no side effects.

When fertility control is used as a means complementary to immunization to reduce contact rate and thereby disease transmission in dog populations, it would be ideal if contraceptives inhibited ovulation, to prevent females in oestrus from attracting males, and aggression and roaming in males. In those cultures where owners of guard dogs support sterilization of males provided that the aggressive behaviour of their animal remains unchanged, preference should be given to targeting female dogs. In any case, given the potential for a single male to fertilize large numbers of females, fertility control programmes should first target females, ideally coupled with parallel treatment of males (Tepsumethanon et al., 2005; Massei et al., 2010). This could be achieved by using contraceptives that are effective on both sexes, or by integrating the use of different drugs, for instance GnRH-based immunocontraceptives and male chemosterilants.

In terms of animal welfare, the incidence and severity of negative side effects of fertility inhibitors should be evaluated at population level, compared to the risks of surgical sterilization and discussed in the wider context of disease elimination. For instance, the fact that a small proportion of dogs might suffer from injection site reaction to a contraceptive should be weighed against the possibility of eliminating a disease such as rabies and thus eliminating rabies-induced welfare costs for dogs, humans, and livestock. In addition, unlike companion animals for which owners expect the contraceptive to be 100% reliable and predictable in duration, fertility control of free-roaming dogs should be evaluated at population level. As such, it is not essential that contraception is effective in all treated animals, but a predictable effect on population size is required (Carroll *et al.*, 2010; Levy, 2011).

The long-term effectiveness of contraceptives has been widely debated: while some see permanent infertility as a prerequisite for field applications of fertility control, others point out that a contraceptive that can render animals infertile for 2–3 years is likely to last the whole lifespan of most free-roaming cats and dogs (ACC&D, 2010; Reece *et al.*, 2008; Budke and Slater, 2009; Levy, 2011).

Efforts to develop fertility inhibitors for free-roaming dogs have multiplied worldwide. Factors responsible for this renewed interest include the availability of new molecular technologies that have allowed the development of novel compounds; the integration of several disciplines such as ecology, economics, and social sciences addressing problems of public health, dogs, and zoonoses; and the growth of emerging economies, such as India, China, and Brazil where conflicts between free-roaming dogs and human interests are widespread and still largely unresolved (e.g. Knobel et al., 2005; Lembo et al., 2010; Zinsstag et al., 2011). In parallel, mathematical models have provided the conceptual framework to evaluate the impact of different dog population management options or disease control strategies in terms of effectiveness, costs, and sustainability (Carroll et al., 2010; Totton et al., 2010; Zhang et al., 2011).

Future development of fertility control compounds will depend on a number of factors including meeting the requirement of regulatory agencies for the use of these compounds on animals and in the environment, and for the safety of operators. Other important factors are the competitive cost of the products, feasibility of delivering fertility control agents to the required proportion of dogs, and the practicality of integrating fertility control with vaccination campaigns.

Few of the many fertility inhibitors that could be used on free-roaming dogs, are commercially available in different countries. Several can be used off-label and many more are at a very early stage of development or testing (Asa and Porton, 2005; ACC&D, 2010; Fagerstone *et al.*, 2010; Cathey and Memon, 2010). The breadth of approaches, the growing commercial interests, and the increasing public pressure for achieving effective, humane, environmentally sensitive, and sustainable population control suggest that non-surgical sterilization will play a key role in disease control and dog population management in the very near future.

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