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Bacterial Zoonoses Transmitted by Household Pets: State-of-the-Art and Future Perspectives for Targeted Research and Policy Actions

P. Damborg*, E. M. Broens†, B. B. Chomel‡, S. Guenther§, F. Pasmans‖, J. A. Wagenaar†, J. S. Weese¶, L. H. Wieler§, U. Windahl#, D. Vanrompay††, and L. Guardabassi*

* *Department of Veterinary Disease Biology, Faculty of Health and Medical Sciences, University of Copenhagen, Frederiksberg, Denmark,* † *Department of Infectious Diseases and Immunology, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands,* ‡ *Department of Population Health and Reproduction, School of Veterinary Medicine, University of California, Davis, USA,* § *Institute of Microbiology and Epizootics, Freie Universität Berlin, Berlin, Germany,* ‖ *Department of Pathology, Bacteriology and Avian Diseases, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium,* ¶ *Department of Pathobiology, University of Guelph, Guelph, Canada,* # *Department of Animal Health and Antimicrobial Strategies, National Veterinary Institute, Uppsala, Sweden and* †† *Department of Molecular Biotechnology, Faculty of Bioscience Engineering, University of Ghent, Ghent, Belgium*

Summary

The close contact between household pets and people offers favourable conditions for bacterial transmission. In this article, the aetiology, prevalence, transmission, impact on human health and preventative measures are summarized for selected bacterial zoonoses transmissible by household pets. Six zoonoses representing distinct transmission routes were selected arbitrarily based on the available information on incidence and severity of pet-associated disease caused by zoonotic bacteria: bite infections and cat scratch disease (physical injuries), psittacosis (inhalation), leptospirosis (contact with urine), and campylobacteriosis and salmonellosis (faecal–oral ingestion). Antimicrobial resistance was also included due to the recent emergence of multidrug-resistant bacteria of zoonotic potential in dogs and cats. There is a general lack of data on pathogen prevalence in the relevant pet population and on the incidence of human infections attributable to pets. In order to address these gaps in knowledge, and to minimize the risk of human infection, actions at several levels are recommended, including: (1) coordinated surveillance of zoonotic pathogens and antimicrobial resistance in household pets, (2) studies to estimate the burden of human disease attributable to pets and to identify risk behaviours facilitating transmission, and (3) education of those in charge of pets, animal caretakers, veterinarians and human medical healthcare practitioners on the potential zoonotic risks associated with exposure to pets. Disease-specific recommendations include incentives to undertake research aimed at the development of new diagnostic tests, veterinary-specific antimicrobial products and vaccines, as well as initiatives to promote best practices in veterinary diagnostic laboratories and prudent antimicrobial usage.

Keywords: antimicrobial resistance; bacterial zoonoses; pet animal

Introduction

The number of pet animals kept within households is increasing and the range of animal species kept for this purpose has extended from traditional household pets such as dogs and cats to encompass rodents, rabbits, ferrets, birds, amphibians, reptiles and ornamental fish. It has been estimated that the population of dogs and cats alone exceeds 127 million in the EU countries (FEDIAF, 2012).

Correspondence to: P. Damborg (e-mail: pedam@sund.ku.dk).

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Household pets, defined here as any animals kept within households by people for company, enjoyment, work or psychological support, can be colonized or infected with a wide variety of bacteria pathogenic to animals and people. Pet-associated bacterial zoonoses represent a relatively neglected area compared with food borne zoonoses. However, the close contact between household pets and people offers favourable conditions for transmission by direct contact (e.g. petting, licking or physical injuries) or indirectly through contamination of food and domestic environments. Indeed, frequent sharing of skin microbiota between people and their dogs has been shown, thus emphasizing the role of contact (Song *et al.*, 2013). Zoonoses are of special concern for people who are young, old, pregnant or immunocompromised, and therefore particularly susceptible to infections. Furthermore, young children may be more exposed to bacteria originating from household pets due to lower hygiene standards and closer physical contact with these animals and the household environment (e.g. floors and carpets).

This paper focuses on selected bacterial zoonoses (Table 1) representing distinct transmission routes, namely bite infections and cat scratch disease (CSD) (physical injuries), psittacosis (inhalation), leptospirosis (contact with urine or urine-contaminated environments) and campylobacteriosis and salmonellosis (faecal–oral ingestion). Selection of these diseases was based on a subjective assessment, considering the available information on the incidence and severity of pet-associated disease caused by zoonotic bacteria. Antimicrobial resistance is included among the selected zoonoses in view of the increasing evidence (Wieler *et al.*, 2011) that household pets are a source of infection of multidrug-resistant (MDR) bacteria of zoonotic potential such as meticillin-resistant *Staphylococcus aureus* (MRSA), meticillin-resistant *Staphylococcus pseudintermedius* (MRSP) and extended-spectrum β-lactamase (ESBL)-producing *Escherichia coli*. Examples of other bacterial diseases reported in pets are shown in Table 2, but are not discussed further. The aim of the paper is to identify targeted research and policy actions to assess and reduce the risk of zoonotic transmission of bacteria from pets. For this purpose, the aetiology, prevalence, transmission, impact on human health and prevention of each selected zoonosis were reviewed.

Bite Infections

Dog and cat bites are frequent injuries among pet owners and those coming into more frequent contact with animals (e.g. veterinarians and animal-related workers and postal workers). Bites are one of the main sources of bacterial infections related to pet ownership.

Aetiology, Transmission and Prevalence

Bites from household pets may result in infections caused by a wide range of bacteria residing on the oral mucosa of the animal and on the skin of the bite victim. The most common bacteria transmitted by cat and dog bites are *Pasteurella multocida* and *Pasteurella canis*, respectively (Talan *et al.*, 1999; Oehler *et al.*, 2009; Patronek and Slavinski, 2009); however, the oral cavity of dogs and cats harbours a diverse microbiota and multiple potential zoonotic pathogens can be found in every animal (Sturgeon *et al.*, 2013, 2014). Dog bites are the most common and account for approximately 80% of all reported animal bites (Patronek and Slavinski, 2009), but cat bites are more likely to develop wound infection due to the puncture lesions caused by the cat's sharper teeth. It has been estimated that 20–80% of cat bite wounds become infected, while infection rates for dog bites are as low as 3–18% (Talan *et al.*, 1999). Bites by rodents can cause rat bite fever associated with *Streptobacillus moniliformis* or, less frequently, *Spirillum minus* (Gaastra *et al.*, 2009) as well as infections caused by a range of other opportunistic pathogens.

Impact on Human Health

Dog and cat bites comprise approximately 1% of accident and emergency department visits in both the USA and Europe (Oehler *et al.*, 2009). In the Netherlands, between 50,000 and 100,000 people are bitten by a pet animal each year (Gaastra and Lipman, 2010), corresponding to 0.3–0.6% of the total population. Factors such as the type of injury, injury location, quantity and type of bacteria, foreign material, wound care and patient health/immune status determine whether bite wounds become infected and the severity of infection (Patronek and Slavinski, 2009).

Capnocytophaga canimorsus is a rare cause of bite wound infection with around 200 cases reported worldwide (Macrea *et al.*, 2008); however, this is probably an underestimate of the impact of this serious infection. This agent can lead to severe bite infections with systemic manifestations such as septicaemia and meningitis. Disease almost always occurs in immunocompromised individuals (particularly individuals without a functional spleen) and alcoholics, and has a mortality rate of about 30% (Lion *et al.*, 1996).

Table 1
Bacterial zoonoses transmissible by household pets and described in this article

Human zoonotic disease	*Pathogen(s) involved*	*Main household pet reservoir**	*Reasons for concern*
Bite wound infections	*Pasteurella multocida* *Pasteurella canis* *Capnocytophaga canimorsus* etc.	Dogs, cats (rodents)	Very high incidence. Risk of therapeutic failure due to inadequate antimicrobial prophylaxis.
Cat scratch disease	*Bartonella henselae* and other *Bartonella* spp.	Cats (dogs, rabbits)	Cats are a natural reservoir with high bacteraemia prevalence in some geographical regions. Lack of information on frequency of human infections (likely underreported). Can result in severe disease in man.
Leptospirosis	*Leptospira* spp.	Dogs, (rats)	Dogs are an important reservoir in some geographical regions. Emerging new serovars in dogs are not covered by vaccines. Epidemiology may be influenced by climate changes (e.g. floods in cities). Can result in severe disease in both man and animals. Highly contagious.
Multidrug-resistant infections†	MRSA MRSP ESBL-producing Enterobacteriaceae MDR *Acinetobacter baumanii*	Dogs, cats	Most of the bacteria have limited host barriers. Truly emerging problem, which is expected to increase. Both human and animal health problem.
Psittacosis	*Chlamydia psittaci*	Birds	Airborne and highly contagious. Lack of information on frequency of human infections (likely underreported). Can result in severe disease in both man and animals. Large outbreaks have occurred (e.g. bird fairs).
Salmonellosis	*Salmonella* spp.	Reptiles (birds, rodents, cats, dogs, fish)	Reptiles are a natural reservoir with very high prevalence. Reptiles have a proven relatively high contribution to human infections, especially in children.

*Potential reservoirs of low or unknown relevance are mentioned in parentheses.
†Only MDR bacteria that are relatively common in household pets and of known zoonotic potential are included here.

Table 2
Examples of bacterial zoonoses for which household pets have limited or unknown importance

Human zoonotic disease	*Pathogen(s) involved*	*Main household pet reservoir**	*Reasons for concern*
Brucellosis	*Brucella canis* *Brucella suis* *Brucella melitensis* *Brucella abortus*	Dogs	Trade of dogs from endemic areas (e.g. Eastern Europe) may impose a risk. Both human and animal health problem.
Chlamydiosis	*Chlamydia felis*	Cats	High prevalence in cats. Affects cat health. Possibly underdiagnosed in man.
Clostridiosis	*Clostridium difficile*	Dogs	Both human and animal health problem. Common in human healthcare and emerging community pathogen. Same strains found in people and animals, with some evidence of interspecies transfer.
Mycobacterial infections	*Mycobacterium* spp.	Fish, cats, birds, (dogs)	High incidence of infection in homeless people and subsequent potential for exposure of pets who might then expose other people (*M. tuberculosis*). Potential problem in immunocompromised people (*M. avium* complex). May cause opportunistic infections in immunocompetent people (*M. marinum*).
Mycoplasma infections	*Mycoplasma haemofelis*	Cats	High prevalence in cats. Possibly underdiagnosed in man.
Tularaemia	*Francisella tularensis*	Cats, rabbits, (dogs)	Both human and animal health problem. Highly contagious.
Q fever	*Coxiella burnettii*	Dogs, cats	Airborne and highly contagious. May cause large outbreaks.

*Potential reservoirs of low or unknown relevance are mentioned in parentheses.

Prevention

Education plays a primary role in prevention of pet bites; owners should be advised by veterinarians on how to interact safely with pets and about the importance of proper socialisation of puppies to reduce aggressive behaviour in adult dogs. When bites occur, basic first aid measures are indicated to prevent infection. Regardless of wound size, antimicrobial prophylaxis is indicated: (1) when bite wounds are located at critical sites (e.g. face, joints and tendon sheaths) and (2) when the bite victim is immunocompromised (Gaastra and Lipman, 2010). Understanding the potential for bite infections and the appropriate medical response is important for attending physicians, to ensure that proper treatment is provided when required.

Specific Research/Policy Recommendations

Bite infection incidence estimates are based mostly on cases registered at hospitals, even though many cases are treated elsewhere. Large-scale multicentre studies are therefore needed to estimate the actual incidence of animal bite infections and their impact on human health (e.g. frequency of treatment failure, complications and economic burden). Monitoring of antimicrobial resistance in bite wound isolates and evaluation of treatment outcomes should form the basis for the development of evidence-based antimicrobial prophylaxis guidelines on bite wound management. Research involving pet interactions and bite avoidance programs, particularly those directed at children, is needed to help reduce the risk of bites.

Cat Scratch Disease

The high prevalence of *Bartonella henselae* in some geographical areas and certain cat populations (e.g. stray and shelter cats), combined with the fact that domestic cats represent one of the largest populations of household pets worldwide, implies a potentially high risk of humans acquiring CSD. The risk of misdiagnosis and the potential development of severe infections in immunocompromised patients are the main concerns regarding this disease.

Aetiology, Transmission and Prevalence

CSD is caused by members of the genus *Bartonella*, a diverse group of blood-borne, gram-negative bacteria. Domestic cats are the natural reservoir of *B. henselae*, which is the main agent of CSD. *Bartonella* bacteraemia is most frequent in stray cats, cats in shelters/catteries and young cats infested with fleas (Boulouis *et al.*, 2005; Chomel *et al.*, 2009; Breitschwerdt *et al.*, 2010). The prevalence of bacteraemia amongst pet cats is generally lower in countries with a cold climate (e.g. 0% in Norway) than in warm, humid countries (e.g. 83% in Thailand) (Boulouis *et al*., 2005; Juvet *et al*., 2010; Ayllón *et al*., 2012). *B. henselae* is generally carried by cats without clinical signs, although some cases of feline endocarditis and stomatitis have been described (Chomel and Kasten, 2010). The cat flea is a vector for transmission between cats, mainly by intradermal inoculation of flea faeces (Chomel *et al*., 1996; Foil *et al*., 1998). Zoonotic transmission from cats to people is likely acquired during scratching by contaminated flea faeces coming into contact with skin abrasions, or indirectly through exposure to faeces of fleas that have fed on infected cats. Transmission is less likely to occur through bites (Chomel *et al*., 2009).

Impact on Human Health

CSD often results in mild, non-specific symptoms such as lymphadenopathy, fever or headaches, but severe clinical manifestations such as encephalitis, angiomatosis and endocarditis may also occur, especially in immunocompromised patients (Chomel *et al*., 2006). The incidence of CSD has been estimated in few European countries. In France and the Netherlands, 7.6 and 11.9 cases occur per 100,000 inhabitants each year, respectively (Chomel *et al*., 2004). This is comparable to the estimated 9.3 cases per 100,000 inhabitants in North America. It has also been estimated that *Bartonella* spp. account for around 3% of all cases of human endocarditis in Europe (Raoult *et al*., 1996). These numbers are based on the number of reported cases and are likely to underestimate the actual incidence of CSD and *Bartonella* infections in people.

Prevention

There are two main aspects to control of CSD. One is reducing exposure in the feline reservoir, which is achieved mainly through flea control. Proper flea control can eliminate the vector and is likely to have a profound effect on the likelihood of transmission from cats to people. The other aspect involves prevention of human exposure, particularly through proper wound care and prevention of scratches and bites, as described in the previous section on bite infections.

Specific Research/Policy Recommendations

There is an overall need for a better understanding of the role of *Bartonella* spp. in human disease. International multicentre studies investigating the prevalence of seropositivity and the incidence of CSD in the general human population, as well as the relative frequency of different clinical pictures, are needed to establish a baseline for further research. Awareness of the disease might be heightened for healthcare practitioners, since CSD is currently severely underreported. Optimizing diagnosis of CSD is also a prerequisite for other initiatives, such as making the disease notifiable. We recommend that the disease becomes notifiable in risk groups (i.e. young, old, pregnant or immunocompromised people) in order to learn more about the consequences of severe infections in these patients.

Psittacosis

Pet birds, particularly those of the psittacine family (e.g. cockatoos, parrots, parakeets and lories), represent an extensive reservoir for *Chlamydia psittaci*, the causative agent of psittacosis or 'parrot fever'. While the incidence of psittacosis appears to be quite low, this infection can be life-threatening and control measures are complicated by potential misdiagnosis.

Aetiology, Transmission and Prevalence

C. psittaci is a gram-negative, obligate intracellular bacterium that may survive in the environment for months in its infectious form (i.e. elementary bodies). At least 465 avian species can be infected with this zoonotic agent (Kaleta and Taday, 2003). Among pet birds, *C. psittaci* is highly prevalent in psittacine birds (16–81%) and pigeons (12.5–95%) (Vanrompay *et al*., 2007; Ling *et al*., in press). Birds may present with respiratory distress or general signs of disease, but more often become persistent carriers without displaying clinical signs (Dickx *et al*., 2010). This status is characterized by the presence of non-replicating aberrant bodies inside cells. On reactivation of replication, the birds shed *C. psittaci* from the respiratory and gastrointestinal tracts (Evans, 2011). Birds are mainly infected after inhalation of *C. psittaci*-containing aerosols or dust; however, avian infection also occurs by vertical transmission, ingestion and via bloodsucking parasites. People are mostly infected after inhalation of *C. psittaci*-infected aerosols or dust, after petting infected companion birds, after handling infected avian tissues or being exposed to *C. psittaci* in excretions (e.g. from cage bedding) (West, 2011).

Impact on Human Health

Populations most at risk include bird owners, pet shop employees, taxidermists and veterinarians. The occupational risk was evident during an outbreak where people in contact with infected birds developed psittacosis and the same *C. psittaci* genotype was detected in affected birds and people (Gaede *et al*., 2008). The course of psittacosis may vary from asymptomatic to a flu-like syndrome and involvement of the respiratory tract. Severe complications such as endocarditis, encephalitis or fetal death are rare. Between 2001 and 2007, fewer than 400 cases were reported annually in Europe with 0–2 fatalities per year (Beeckman and Vanrompay, 2009). However, these numbers are likely underestimated due to unrecognized cases.

Prevention

Currently no effective vaccine exists for avian chlamydiosis. Guidelines for control of psittacosis are available from the US National Association of State Public Health Veterinarians (NASPHV; http://www.nasphv.org). Key measures include good husbandry practices, such as regular cleaning of cages, avoiding spread of feathers, dust and litter between cages, and quarantine of diseased or newly purchased birds. Birds may be screened for antibodies specific for *Chlamydia* spp., for example if they have frequent public contact or prior to trade. People handling sick birds or cleaning their cages should wear protective clothing.

Specific Research/Policy Recommendations

Better diagnostic tools are needed to elucidate the role and frequency of *C. psittaci* in human disease. At present, serological tests are often used for diagnosis of *C. psittaci* infection in birds. However, serology cannot provide a definitive diagnosis due to the lack of specific antibody detection assays, the high 'background' in endemic bird populations, the long persistence of antibody titres in cured birds and the need for convalescent sera to detect seroconversion. There is a need to validate newly developed nucleic acid amplification techniques, such as polymerase chain reaction (PCR), for rapid detection of infected animals and for diagnosis of infection in human patients (Vanrompay, 2013). A vaccine targeting pet birds would have a huge impact on prevention of psittacosis.

Leptospirosis

Human exposure to *Leptospira* spp. has traditionally been associated with direct or indirect contact with wildlife. However, the re-emergence of *Leptospira* spp. in pet populations in some geographical areas, and the potential severity of this infection, are reasons for concern.

Aetiology, Transmission and Prevalence

Leptospirosis is caused by members of the genus *Leptospira*, a diverse group of gram-negative bacteria that can survive for long periods of time in warm, wet environments. Virtually any domestic animal species can be infected, and different serovars may be involved depending on the animal species. Serogroup distribution in dogs varies widely. The major serogroups to which dogs in Europe are exposed are Icterohaemorrhagiae, Grippotyphosa, Australis, Sejroe and Canicola (Ellis, 2010). Leptospirosis is considered a re-emerging disease in dogs and is endemic in many countries. Prevalence rates reported in different regions are difficult to compare because of methodological differences between studies. One common trend is that the highest seroprevalence rates (up to 84%) are observed in stray and kennelled dogs (Jittapalapong *et al*., 2009). Risk factors for seropositivity or disease in dogs include exposure to wildlife, being a working, herding or hound dog, being >5 years of age and living in peri-urban or urban areas (Ward *et al*., 2002; Alton *et al*., 2009; Hennebelle *et al*., 2014). However, the changing incidence has also been accompanied by anecdotal changes in at-risk populations and risk factors in some regions, with increases in disease concentrated on urban dogs, potentially as a consequence of changes in urban wildlife numbers and infection rates. While much less common, leptospirosis can occur in cats, particularly stray cats (Millán *et al*., 2009). Important serovars of *Leptospira* can also occur in pet rats, although the prevalence is unknown (Gaudie *et al*., 2008). Animals are often silent carriers of leptospires, but mild to severe infection may develop, most commonly in the urinary tract. Transmission occurs through ingestion or contact of leptospires with mucous membranes or broken skin (Levett, 2001). Most infections are acquired from urine-contaminated environmental sources, particularly water.

Impact on Human Health

The reported incidence of human infection in most countries is low, such as the 0.06/100,000 people incidence rate reported in Germany (Jansen *et al*., 2005). Such figures likely represent a large underestimation of the actual incidence due to the problems of diagnosis associated with non-specific symptoms and the lack of diagnostic tests with high sensitivity. Most human infections are mild (e.g. rash, headache and lymphadenopathy) or asymptomatic, but severe cases of hepatic or renal failure (Weil's disease) are not infrequent, especially in risk groups (i.e. young, old, pregnant and immunocompromised). Despite the fact that people are often affected by the same serovars as dogs (Dupouey *et al*., 2014), the overall contribution of these animals to the burden of human leptospirosis is thought to be limited. Zoonotic transmission from dogs is poorly documented and largely involves anecdotal or poorly documented reports (Allard and Bedard, 2006; Vincent *et al*., 2007). The risk is likely greatest for owners and veterinary personnel exposed to acutely ill animals and laboratory personnel exposed to blood, urine or tissue samples from patients. Pet rat owners may be the main risk group for pet-associated leptospirosis, since wild rats are the main reservoir for *Leptospira icterhaemorrhagiae*, the most human pathogenic *Leptospira* serovar (Gaudie *et al*., 2008; Dupouey *et al*., 2014).

Prevention

Vaccines for dogs generally protect against the serovars *L. canicola* and *L. icterohaemorrhagiae*, and some of them additionally provide protection against region-specific serovars. Suspected animal patients should be isolated and antimicrobial treatment should be initiated promptly. For all categories at risk, especially in endemic areas, general hygiene practices associated with handling of animals or contact with dog urine are critical considering the occurrence of healthy carriers and the vague nature of the clinical signs at early infection stages. Human risk groups (see above) should be particularly aware of the risks associated with handling of pet rats.

Specific Research/Policy Recommendations

Serology is commonly used for diagnosis of leptospirosis; however, most serological tests are suboptimal in clinical practice because of the time required (i.e. weeks to obtain convalescent titres), false-positive results due to vaccination and cross-reaction between different serotypes. Serology has therefore partially been replaced by DNA-based tests for detection of *Leptospira* spp. in dog urine or blood. Apart from facilitating diagnosis, and thereby proper infection control practices and early treatment, reliable DNA-based tests will facilitate future research to determine the prevalence of subclinical carriers and to evaluate the efficacy of different antimicrobial treatment strategies. Vaccines for dogs should be continuously validated for their efficacy, and new vaccines should be developed to ensure coverage of region-specific serovars.

Campylobacteriosis

Campylobacteriosis is predominantly a food-borne disease, but there is clear evidence of zoonotic transmission from pets. Current evidence suggests that transmission from household pets accounts for a minority of human cases.

Aetiology, Transmission and Prevalence

Dogs and cats are well-recognized carriers of *Campylobacter*, a gram-negative genus associated with human gastroenteritis. Carriage rates may reach figures up to 50% in healthy dogs and cats, with relatively higher rates in puppies and kittens and in stray and kennel populations (Baker *et al*., 1999; Wieland *et al*., 2005). *Campylobacter upsaliensis* is the most common species, followed by *C. jejuni*. Other household pets (e.g. rodents and reptiles) are potential carriers of *Campylobacter*, but prevalence data are sparse (Skirrow, 1994; Gilbert *et al*., 2014). Pet animal carriers often do not manifest clinical signs of disease, although cases of diarrhoea in young animals <1 year of age, have been associated with the presence of *Campylobacter* (Burnens *et al*., 1992). Transmission occurs by the faecal–oral route, either directly or indirectly via fomites such as contaminated food and water.

Impact on Human Health

Campylobacteriosis is a leading cause of gastroenteritis in industrialized countries (Humphrey *et al*., 2007). The most common symptom is diarrhoea, which in 0.15% of cases develops into septicaemia. *C. jejuni* is the most common *Campylobacter* species isolated from human patients. Although food, in particular poultry, is the main source of infection, various epidemiological studies have also identified contact with pets as a risk factor for campylobacteriosis (Mughini Gras *et al*., 2013). Stafford *et al*. (2008) estimated that approximately 3% of cases of human campylobacteriosis could be attributed to ownership of puppies and Buettner *et al*. (2010) estimated that 8% of cases of human campylobacteriosis might be due to contact with cats and dogs. Case-based studies have identified indistinguishable *C. jejuni* clones in human patients and their dogs (Wolfs *et al*., 2001; Damborg *et al*., 2004), but such studies are rarely able to infer the direction of transmission. *C. upsaliensis* is believed to play a minor role in human disease, but the frequency of infections caused by this species might be underestimated by some diagnostic laboratories, since it requires special growth media that are not used routinely.

Prevention

Prevention of campylobacteriosis relies on avoidance of direct or indirect exposure to animal faeces. As such, the main preventive measures include proper handling of pet faeces and litter box management, removal of faeces from public areas, and hand hygiene after contact with pets and pet-contaminated items.

Specific Research/Policy Recommendations

Large-scale risk studies may identify human behaviours increasing the risk of *Campylobacter* spp. transmission from pets and further research would be necessary to assess the incidence of human infections with *C. upsaliensis*.

Salmonellosis

Reptiles are considered a reservoir of *Salmonella* spp. and constitute a significant source of human nontyphoidal salmonellosis. Reptile-acquired salmonellosis (RAS) often presents as a severe invasive disease, especially in young children. Since the role of other companion animals in transmission of *Salmonella* spp. to people is unclear and probably of less concern, this section will primarily focus on RAS.

Aetiology, Transmission and Prevalence

Salmonella is a gram-negative bacterium, which can survive for weeks to months in the environment, in particular in warm and moist places. Among household pets, reptiles belonging to all major extant orders (i.e. crocodilians, lizards, snakes and chelonians) constitute the most important reservoir. A wide variety of primarily non-host adapted *Salmonella* serovars are isolated from these animals. This includes several exotic serovars mostly related to reptiles (e.g. *S. poona*) and serovars that are well-established in people, but more often associated with transfer from food animals (e.g. *S. typhimurium*) (Pedersen *et al.*, 2009). *Salmonella* is generally considered a normal constituent of the reptilian intestinal microbiota, since cumulative prevalence studies often show rates approaching 100% (Hoelzer *et al.*, 2011). Clinical salmonellosis is rare in reptiles and is generally provoked by an underlying primary cause of disease, but might present as salpingitis or septicaemia (Pasmans *et al.*, 2008).

Data on the occurrence of *Salmonella* in other household pets are generally sparse. Prevalences ranging from 0 to 9% and 0 to 4% have been reported in dogs and cats, respectively (Marks *et al.*, 2011). However, much higher prevalences may be identified in stray or shelter cats/dogs as well as dogs fed raw food diets (Marks *et al.*, 2011). Dogs, cats and most other non-reptile household pet species are primarily infected subclinically, but infections ranging from mild (e.g. fever of unknown origin) to potential, fatal gastroenteritis and septicaemia can occur (Marks *et al.*, 2011). *Salmonella* is transmitted directly or indirectly by the faecal–oral route as described for *Campylobacter*.

Impact on Human Health

Most people infected with *Salmonella* spp. develop symptoms of gastroenteritis. Depending on the age or the immune status of the patient and the serovar involved, salmonellosis may evolve to septicaemia, abortion and even death. Children <5 years of age are particularly at risk of RAS, probably due to the combination of their higher susceptibility to infection, greater contact with pets and limited hygiene practices (Aiken *et al.*, 2010). In the 1970s, chelonians were the source of 11–22% of all registered cases of human salmonellosis (Lamm *et al.*, 1972; Cohen *et al.*, 1980). In 1975, the sale of small turtles was prohibited in the USA, which resulted in an estimated annual reduction of 100,000 *Salmonella* infections in children (Cohen *et al.*, 1980). A more recent case–control study estimated that 6% of all sporadic *Salmonella* infections in the USA can be attributed to reptiles or amphibians (Mermin *et al.*, 2004), while a case–case study estimated reptile exposure to account for 0.95% of *Salmonella* cases in the UK (Aiken *et al.*, 2010).

Other pet animal species appear to play a less important role in human salmonellosis, with only a few published cases of confirmed transfer from cats, dogs, rodents, a parakeet, amphibians, aquarium fish and non-traditional mammalian pets (e.g. hedgehogs) (Hoelzer *et al.*, 2011). One case–control study reported cat exposure, as well as reptile contact, to be a risk factor for childhood salmonellosis (Younus *et al.*, 2010).

Prevention

The ubiquitous presence of *Salmonella* in reptiles makes it difficult to eradicate this bacterium. Instead, focus should be on minimizing human exposure. A guideline published by the Association of Reptilian and Amphibian Veterinarians (http://www.arav.org/special-topics/) recommends that risk groups (i.e. young, old, pregnant and immunocompromised people) should avoid direct and indirect contact with reptiles, while other people in contact with reptiles must focus on good hygiene measures, particularly hand hygiene. Hygiene precautions should also be taken when handling feeder mice, which can be a reservoir for *Salmonella* (Harker *et al.*, 2011). Less stringent hygiene measures can probably be used to prevent transmission from other household pets. Feeding raw diets to carnivores should be limited as they are more likely to have *Salmonella* compared with commercial dry diets (Hoelzer *et al*., 2011).

Specific Research/Policy Recommendations

An apparent link between stress and *Salmonella* shedding (Verbrugghe *et al*., 2012) suggests that husbandry practices could be optimized to reduce shedding. Further research is needed to evaluate whether this approach can be used to reduce human exposure to *Salmonella*, while improving animal welfare of reptiles kept in captivity. Minimizing exposure of dogs and cats to *Salmonella* spp. would require the creation of international pet food industry standards for raw pet food and raw animal-based pet treats, including the use of processing practices (e.g. high pressure pasteurization, irradiation) to reduce or eliminate contamination.

Antimicrobial Resistance

There is increasing concern about the rapid emergence and spread of MDR bacteria among household pets in recent years. Various genetic similarities have been observed between MDR isolates from human infections and from household pets. This implicates a zoonotic risk, which is further supported by recent studies indicating contact with pets as a risk factor for human infections with resistant bacteria, and by several case reports suggesting household transmission of resistant strains between pets and their owners.

Aetiology, Prevalence and Transmission

During the last decade, various MDR bacteria such as ESBL-producing *E. coli*, MRSA and MRSP have spread among dogs and cats on a worldwide basis (Guardabassi *et al*., 2004; Wieler *et al*., 2011; Ewers *et al*., 2012). Multidrug resistance has also appeared in other bacterial pathogens encountered in small animal practice, including typical human nosocomial pathogens such as carbapenemase-producing *E. coli* and MDR *Klebsiella pneumoniae* and *Acinetobacter baumannii* (Müller *et al*., 2014; Woodford *et al*., 2014). All of these MDR bacteria can be hospital-acquired, and resistant to virtually all conventional antimicrobials licensed for animal use. Hospitalization and antimicrobial treatment, especially with broad-spectrum drugs such as cephalosporins and fluoroquinolones, are major risk factors associated with carriage and infection with MDR bacteria in animals (Weese and van Duijkeren, 2010). The prevalence of MDR bacteria in the pet population varies considerably between countries. The reason for this geographical variation is unclear, but it is likely related to local variations in patterns of antimicrobial use. Zoonotic transmission from infected or colonized pets to people can occur by direct contact or indirectly through environmental contamination of households, veterinary clinics and public spaces. It should be noted that human-to-pet transmission may also occur. The risk that pets acquire MRSA from people is particularly high, since the MRSA types found in dogs and cats often correspond to widespread clones in the local human population (Vincze *et al*., 2014).

Impact on Human Health

Significant public health concerns exist because of the possible risk of animal-to-human transmission of resistant clones and/or resistance genes. Exposure to companion animals has been identified by two separate studies as a risk factor for ESBL carriage in people (Meyer *et al*., 2012; Leistner *et al*., 2013). Other evidence supporting a role for household pets in human ESBL infections include the occurrence of specific ESBL-producing *E. coli* clones (e.g. B2-O25b:H4-ST131 and CTX-M-15-ST648) and ESBL types (e.g. CTX-M-15 and CTX-M-1) in both people and pets (Ewers *et al*., 2012). MRSA colonization (and perhaps infection) is a recognized occupational risk in veterinary staff and various studies have identified the same MRSA strains in people and pets sharing the same household (Weese, 2010). Although the most common MRSA clones infecting or colonizing pets (e.g. ST22) occurred in people a long time before their emergence in pets, and are likely to originate from man, pets may serve as infection sources for MRSA infection or (re)colonization of human patients (Loeffler and Lloyd, 2010). Considering that *S. pseudintermedius* has a canine origin and is not a commensal in people, the relatively high MRSP carriage rates (up to 8%) among owners of infected dogs and veterinary personnel provide indirect evidence of zoonotic transmission (Ishihara *et al*., 2010; Walther *et al*., 2012). MRSP infections have been reported in dog owners and their frequency may be underestimated due to diagnostic problems regarding identification of *S. pseudintermedius*, and consequently MRSP, in human clinical microbiology laboratories (Pottumarthy *et al*., 2004). The occurrence of MDR bacteria in household pets has induced veterinary use of critically important antimicrobials (CIAs) authorized for human use only (e.g. carbapenems and glycopeptides) (Weese, 2006, 2008), which may further aggravate the problem. In addition to the risks of zoonotic transmission, untreatable MDR infections in household pets have negative emotional and social effects on the owners and their families (Bengtsson and Greko, 2014).

Prevention

Considering that hospitalization and antimicrobial treatment are the main risk factors for colonization and infection with MDR bacteria, hospital infection control and rational antimicrobial use are essential measures to prevent further spread of MDR bacteria in household pets and, ultimately, to reduce the risk of zoonotic transmission to people. Veterinarians play an important role in educating the owners of patients infected with MDR bacteria to follow best hygiene practices for prevention of zoonotic transmission. Both veterinarians and physicians should raise awareness about the risks of zoonotic infection, especially among risk groups (i.e. young, old, pregnant and immunocompromised people).

Specific Research/Policy Recommendations

Veterinary use of CIAs licensed for human use only must be reduced to an absolute minimum and regulated by legislation. Use of broad-spectrum antimicrobials licensed for veterinary use (e.g. cephalosporins and fluoroquinolones) should be controlled by implementation of antimicrobial stewardship programmes at both the national and the clinic level (Guardabassi and Prescott, 2015). Development of new narrow-spectrum, veterinary-specific antimicrobial products, including anti-infective biological agents such as phage and bacteriocins, is urgently needed for treatment of MDR infections in household pets.

Concluding Remarks

This paper summarizes the present knowledge of selected bacterial zoonoses transmissible by household pets, highlighting important research and policy actions needed to assess and reduce the zoonotic risks derived from exposure to pets. It is clear that the zoonotic risks attributable to household pets are difficult to quantify due to a multitude of knowledge gaps, mainly because most knowledge of the zoonoses transmissible by household pets relies on case reports. Large-scale case–control studies, including cases and matched, healthy controls, are needed to identify human–pet interactions that pose a risk for human disease. Population attributable fractions should be calculated to understand the relative contribution by household pets to zoonoses that may also be acquired from other sources.

For most bacterial zoonoses, there is a lack of baseline data on pathogen prevalence and antimicrobial susceptibility in the relevant pet population. Adequate surveillance of pet-associated zoonoses in

Table 3
Diagnostic challenges concerning the bacterial zoonoses in this article

Pathogen	*Diagnostic challenges*
Antimicrobial-resistant bacteria	Missing or insufficient veterinary-specific clinical breakpoints (bacterial species, animal host and infection-specific breakpoints).
	No global standards for antimicrobial susceptibility testing hampers surveillance and inter-laboratory comparison of data.
	Some carbapenemase-producing bacteria can be difficult to recognize by antibiograms.
Bartonella spp.	Slow growth and special growth requirements.
	Serology is suboptimal because of cross-reaction between species.
	Healthcare personnel often unaware of disease and symptoms often non-specific.
	Reliable PCR/antigen-based methods available mainly in specialized laboratories.
Campylobacter upsaliensis	Failure to grow on conventional agar media used for *Campylobacter* isolation in diagnostic laboratories.
	Some medical microbiologists unaware of the species.
Chlamydia psittaci	Only culturable in cell cultures.
	Serological tests suboptimal clinically because of: (1) the high background in endemic bird populations, (2) the long persistence of antibodies in cured birds, (3) cross-reaction to other bacterial species, and (4) need for convalescent sera to detect seroconversion.
	Healthcare personnel often unaware of disease and symptoms often non-specific.
	Current PCR/antigen-based methods need to be validated.
Leptospira spp.	Shedding only for limited period during disease.
	Very slow growth in conventional media (up to several months).
	Serological tests are suboptimal clinically due to: (1) the long time that is often required to obtain convalescent titres, (2) cross-reaction between different serotypes, (3) poor immune response elicited by especially host-adapted serovars.
	Symptoms often non-specific.
	Reliable PCR/antigen-based test available mainly in specialized laboratories.
Staphylococcus pseudintermedius	Can be misidentified as *S. aureus* by basic phenotypic tests. By MALDI-TOF the species is difficult to distinguish from other *S. intermedius* group (SIG) species.
	Some medical microbiologists unaware of the species.

large regions like Europe would require a centrally coordinated network collecting data from individual countries. Initially, mandatory reporting for selected zoonotic agents that are already reportable in people would be optimal to identify common geographical or temporal trends in people and pets. In the absence of such a network, data can be collected online by voluntary reporting from veterinary clinics and diagnostic laboratories. The Small Animal Veterinary Surveillance Network (SAVSNET, http://www.savsnet.co.uk) and the Worms and Germs Blog (http://www.wormsandgermsblog.com) are examples of successful online initiatives developed recently to collect and share information on infectious diseases in companion animals.

Proper diagnostic tests of high sensitivity and specificity provide an essential basis for any surveillance and research activities recommended in this paper. Various pitfalls regarding the methods used for diagnosis of the pet-associated zoonoses were identified and reviewed (Table 3). Research is needed to develop new rapid and reliable diagnostic tests, as well as to improve the performance of those currently available. Certification of diagnostic laboratories and definition of minimum quality standards are required to ensure best practices in veterinary diagnostic laboratories, including in-house diagnostic facilities located within veterinary clinics.

Finally, education is another key element for reducing the zoonotic risks associated with household pets. Certain zoonotic infections transmitted by household pets, such as CSD, psittacosis and MRSP infections, may be underdiagnosed by physicians. This is partly due to insufficient diagnostic tools, but also to the lack of awareness by primary healthcare practitioners about zoonoses transmitted by companion animals and difficulties of communication between veterinary and medical practitioners. The necessary space and attention should be given to companion animal zoonoses in medical and veterinary university curricula as well as in continuing education, for example by organizing joint courses and seminars for veterinarians and doctors. Education about the zoonotic risks associated with household pets should be extended to animal caretakers and pet owners, who often do not perceive pets as possible sources of infections, indirectly increasing exposure and infection risks.

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Conflict of Interest Statement

The authors declare no conflicts of interest.

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