Infectious Hazards from Pets and Domestic Animals

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1 Introduction

Most pet owners consider their pets to be family members. Approximately 63% of US households own at least one pet [1], and statistical analysis done in the United States in 2006 showed that there are more than 72 million pet dogs and nearly 82 million pet cats, with an average veterinary expenditure per household for all pets of around $366/year [2]. According to a survey conducted by the American Animal Hospital Association (2002), 94% of pet owners consider their pet to have human personality traits, 93% say that they would risk their own life for their pet, and half said that they would choose their dog as their sole companion if stranded on a Desert Island [3]. As a consequence, people tend to treat the health of their pets as they would with their own children and spend more money at the veterinary clinic. This also involves purchasing treatment with broad-spectrum antibiotics.

Pets serve valuable social roles in society, and studies have shown that pet owners had significantly lower systolic blood pressure, reduced cholesterol and triglyceride levels than non-pet owners, and had less feelings of loneliness, while increasing opportunities for exercise, outdoor activities, and socialization [4]. Despite these benefits, pets present zoonotic risks, especially for immunocompromised hosts [5].

Animal to human transmission of infections has been documented to occur through direct contact with an infected animal or through contact with infectious saliva that contaminate bite wounds, skin abrasions, or mucous membranes and through hand-to-mouth transfer of microorganisms, cysts, or oocysts from feces of an infected animal [6].

Other ways of transmission of animal to human infections include aerosol transmission from body fluids (e.g., Q fever) and vector-borne diseases (e.g., Lyme disease, Babesiosis, and Ehrlichiosis). Children are considered at highest risk for infection from pets because they are more likely to have close contact with pets

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and thus more vulnerable to bites and scratches from them. Children are more likely to put objects in their mouth that provides closer contact with the household environment contaminated by pets.

New pets are considered of more health risk than established pets, especially imported ones, since their health history and vaccination records may not be known, while older pets are generally safer than younger ones because they are less likely to be involved in playful activities and thus less biting and scratching [6].

Over and beyond the usual ways of looking at zoonotic infectious hazards, pets and domestic animals afford opportunities for emerging infectious disease threats and a vehicle for the spread of antibiotic-resistant organisms.

2 Global Trends in Emerging Infectious Diseases (EID)

The past two decades have seen the emergence of pathogenic infectious diseases that are associated with a range of underlying causal factors [7]. These include interactions with zoonotic pathogens within the continuum between wildlife, domestic animal, and human populations [8] (Fig. 1).

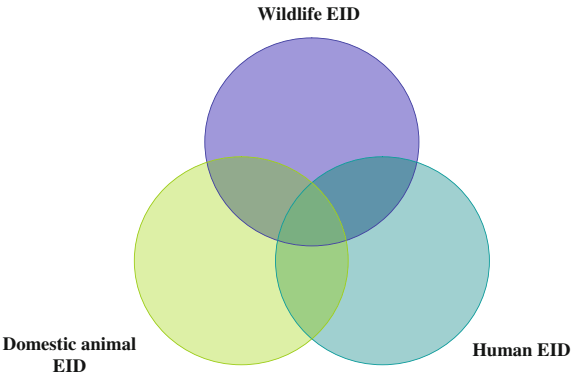

Fig. 1 Most emerging infectious diseases (EID) exist within a host and an infectious agent (parasite) continuum between wildlife, domestic animal, and human populations

In a dramatic study, Jones et al. analyzed the emergence of 335 infectious diseases between 1940 and 2004. A majority (60.3%) of these emerging infectious diseases were zoonoses [9] and 72% of these originated in wildlife (Fig. 2). Data show that those pathogens regarded as emerging and reemerging were more likely to be zoonotic than those that are not [10]. And zoonotic species are overall twice as likely to be associated with emerging disease than non-zoonotic species [11].

About 54.3% of pathogens involved in EID were bacteria and rickettsia (with drug-resistant strains), 25.4% were viral pathogens, 10% were protozoa, 6.3% were fungi, and 3.3% were helminths [9] (Fig. 3). Antimicrobial-resistant microbes constituted 20.9% of these EID and have significantly increased with time

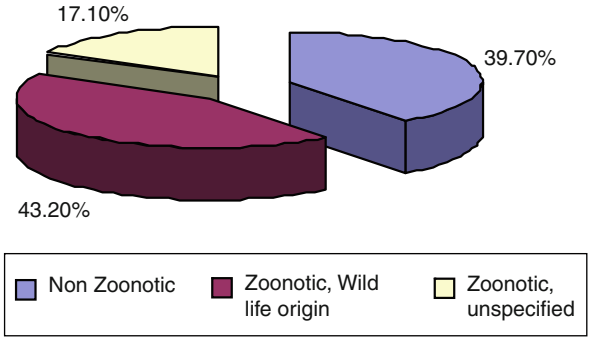

Fig. 2 A pie presentation showing that 60.3% of EID are transmitted by zoonotic pathogens and that wildlife constitutes 71.8% of zoonotic infections (43.20% of overall EID)

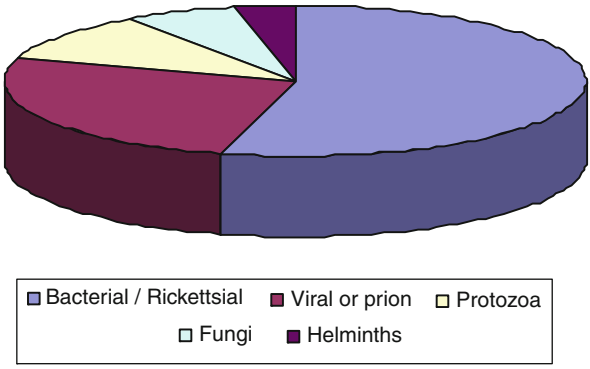

Fig. 3 The EID plotted by different pathogen types

($P < 0.05$). This is thought to be related to the rise in antimicrobial drug use, especially in developed countries [9].

Jones et al. point out that surveillance and reporting of these EIDs are biased. The risk "hot spots" of emergence are in lower latitude developing countries whereas the surveillance resources are in more well-off countries where emergence of such infections is less likely [9]. They advocate for re-allocation of these resources so that they are available in areas where zoonoses will emerge. Wildlife zoonotic EIDs relate to species richness in such parts of the world. EIDs that emerge in the developed world such as antibiotic-resistant organisms tend to be non-wildlife related and are partially driven by population density.

Although zoonotic pathogens do represent the most likely source of emerging and reemerging infectious disease, only small minorities have proved capable of causing major epidemics in the human population [10], and closer collaboration between medical and veterinary researchers is needed for the management of these pathogens.

3 Pets and Domestic Animals as Reservoirs of Antimicrobial Resistance (AMR)

The widespread use of antibiotics in human medicine and agriculture and the related growing problem of bacterial resistance to antibiotics provide a rich area for study and debate. Most of the rising antimicrobial resistance problems in human medicine are due to the overuse and misuse of antimicrobials [12].

Use of antimicrobial agents for nonhumans includes application for a variety of purposes: in production of food animals (livestock, poultry), aquaculture, plant and crop protection, food production, and industrial use, such as the cleaning of oil pipes. At sub-therapeutic levels, antimicrobials are used for growth promotion in livestock and poultry, at varying levels for prophylaxis and at therapeutic levels for treatment.

In addition there has been an increased attention devoted to small animal welfare, with increased expenditure on veterinary care, and prevention and therapy of infectious diseases resulting in the frequent use of antimicrobial agents in pet animals [13], and in particular, broad-spectrum agents such as clavulante-potentiated aminopenicillins, cephalosporins, and fluoroquinolones [14]. All of these ways of exposure, either directly or indirectly, might position pets and domestic animals to develop an inevitable and irreversible antimicrobial resistance, which is a natural consequence of bacterial cell adaptation to exposure to antimicrobial agents.

Bacterial resistance can result from changes in the antibacterial's target or from bypassing of that target, or it can occur as a result of impermeability, efflux pumping, or enzymatic deactivation. Some bacteria are inherently resistant. In others, resistance may arise via hypermutation or horizontal gene transfer by plasmids and transposons [15].

Another mechanism of bacterial resistance is biofilm formation, especially in cases of implant infections, urinary tract infections, and cystic fibrosis [16].

Rapid spread of genes resistant to antimicrobial agents can occur in a bacterial population and from one ecosystem to another. Particular antibiotic resistance genes first described in human-specific bacteria have been found in animal-specific species of microorganisms and vice versa, suggesting that bacterial populations can share and exchange these genes [13].The development of resistance in one bacterial population can spread to other populations over time (Fig. 4).

A recent review suggested that <4% of antimicrobial resistance problems in humans could be associated with animal sources and that this resistance is largely related to zoonotic organisms [17].

Several longitudinal studies conducted at veterinary hospitals have indicated antimicrobial resistance to various agents has emerged among pet animal isolates of *Staphylococcus intermedius*, *Escherichia coli*, and other bacteria with potential for zoonotic transmission and resistance phenotypes, such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and multidrug-resistant *Salmonella typhimurium* DT104 [13].

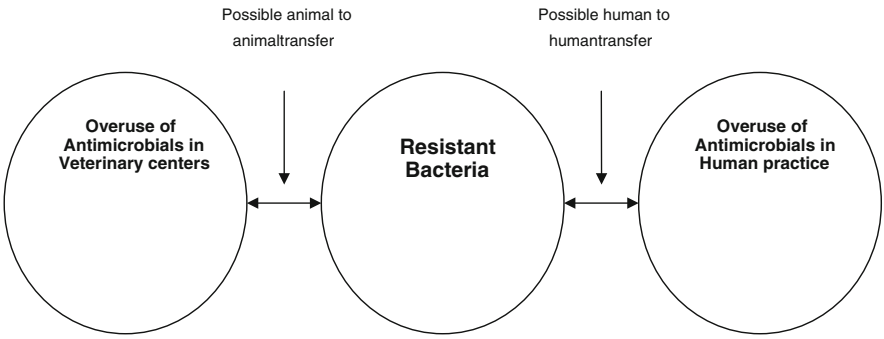

Fig. 4 Schematic representation of the consequences of antimicrobial overuse in animal veterinary practice and human medicine on exchange of resistant bacteria and resistance genes between pet animals and humans

The same applies to food animals, where food production and distribution may represent a dynamic environment for the continuing transfer of antibiotic resistance between bacteria. The widespread use of antibiotics in food animal production has resulted in the emergence of antibiotic-resistant bacteria that can be transmitted to humans through the food chain [18, 19]. In such animals, antimicrobials are used for treatment and illness prevention as well as for growth promotion purposes.

Antimicrobials used for food animal treatments include amoxicillin, erythromycin, gentamicin, tylosin, fluoroquinolones, and sulfonamides [20]. An example of the food-borne transmission of resistant strains is zoonotic apramycin and gentamicin cross-resistance, when apramycin (an aminoglycoside) was introduced as a veterinary antimicrobial in the 1980s to France. A few years later, cross-resistance to both apramycin and gentamicin was detected in *E. coli* and *S. typhimurium* strains isolated from cattle and sheep flocks, which was found to be a plasmid-mediated mechanism of resistance. Between 1985 and 1988, nosocomial human isolates of *E. coli*, *S. typhimurium*, and *Klebsiella pneumoniae* infections were recovered from hospitals that shared the same resistant strains [21].

Some of the growth promoters used belong to the glycopeptides and streptogramins groups, which are essential drugs in the treatment of invasive staphylococcal or enterococcal infections in humans. Research has shown that resistance of these bacteria to classic treatment in humans is often a consequence of the use of antimicrobials in food promotion. The exposure of humans to bacteria resistant to antimicrobials and to resistant genes through food can be reduced effectively by intervention [22].

4 *Staphylococcus intermedius* in Pets

Staphylococcal infections in pets are predominantly caused by *S. intermedius*, with *S. aureus* representing <10% of clinical staphylococcal isolates from dogs and cats. [23, 24].

S. intermedius has been considered as one of the major coagulase-positive species of staphylococci commencing on the skin and mucosal surfaces of canines and is considered the principal cause of canine pyoderma and may cause sepsis and shock in dogs [25].

In humans, *S. intermedius* is rarely associated with severe clinical disease and transmission from dogs does not appear to cause a serious risk for human health. The reported prevalence of *S. intermedius* infection among hospitalized patients is only 6×10^{-4} [26]. However, *S. intermedius* can be a responsible pathogen for some canine-inflicted human wound infections, thus representing a zoonotic pathogen [27]. The possible transmission of *S. intermedius* from dogs to humans was previously reported [28], and there is good evidence from molecular typing studies that it can be transferred the other way between humans and animals also [29]. Man and canine carry the same strains of *S. intermedius* and probably act as a reservoir for these strains. Indeed, the domestication of the dog and the increasing physical relationships between man and dogs may have led to the original zoonotic spread of the organism.

There has been increased prevalence of multidrug-resistant *S. intermedius* strains in pet animals from 11 to 28% between 1986–1987 and 1995–1996 in France [30], with reported resistance to penicillin, neomycin, sulfonamides, and erythromycin between 1980 and 1999–2000 in Switzerland [31]. Guardabassi et al. reported the carriage of *S. intermedius* by 7 out of 13 owners of dogs with pyoderma, where six of the isolated strains from the dog owners were identical to the strains in their dogs and all strains were resistant to up to five antimicrobial drugs, and he also reported that the occurrence of *S. intermedius* in dog owners was significantly higher compared with the non-animal owner control group ($P = 0.03$), which supports the association and possible transfer of *S. intermedius* from dogs to human [29].

In 2007, Loeffler et al. reported the first multiresistant, mecA-positive *S. intermedius* in Europe, where mecA-positive methicillin-resistant *S. intermedius* (MRSI) was isolated from 11 dogs and a cat in Europe. The presence of the gene conferring resistance to all β-lactam antibiotics (mecA) was demonstrated and confirmed by Pulsed Field Gel Electrophoresis (PFGE) and Polymerase Chain Reaction (PCR) testing [32].

Recently, mecA-positive MRSI transmission between animal and human has been reported, where multiresistant MRSI was isolated from infected surgical wounds of five dogs and a cat at the Veterinary Microbiological Diagnostic centre in Netherlands. MRSI with the same resistance pattern was cultured from the nose of a surgeon, three technicians, four environmental samples, and a healthy dog of a staff member in the same clinic. All isolates were proved to be mecA positive by PCR, and PFGE profile done on 13 out of the15 isolates showed that the isolates were indistinguishable [33].

One implication of the transfer of coagulase-positive staphylococci between owners and pet dogs is of the potential transfer of antibacterial resistance between *S. intermedius* and *S. aureus*; as it has been reported previously that canine *S. intermedius* and human *S. aureus* strains share the same tertracyclin resistance genes and

structurally related plasmids which can be mobilized or transduced between members of the same or related staphylococcal species and possibly between animals and humans without knowing the exact direction of transmission [34].

Since antimicrobial resistance is one of the most important emerging public health problems for the future, the veterinary profession needs to monitor trends in antimicrobial use in pets and avoid overuse in order to limit the emergence of multiple antimicrobial resistance in *S. intermedius* and the potential transfer of resistance genes to human staphylococci.

5 MRSA in Pets and Domestic Animals

Methicillin-resistant *S. aureus* (MRSA) is an important worldwide cause of human infections both community acquired and nosocomial. It can cause a wide range of conditions from mild skin and soft tissue infections to life-threatening bacteremias. Recently, infections with MRSA have been increasingly reported as an emerging problem in veterinary medicine, particularly in small animal and equine practices. It has been reported in horses [35], dogs [36], cats [37], chickens [38], cows [39], and pigs [40].

Several reports have presented information suggesting that animals may serve as reservoirs for MRSA infection of humans. In 2005, Loeffler et al. demonstrated that 18% of 78 staff members and 9% of 45 hospitalized dogs in a small animal veterinary referral hospital were carriers of MRSA. After PFGE typing, around 82% of the isolates recovered were indistinguishable or closely related to EMRSA-15 (the predominant strain responsible for human nosocomial infections in the UK) [41].

Manian et al. reported recurrent MRSA infection in a patient with diabetes and in his wife. Decolonization was unsuccessful despite repeated attempts. Sampling of the nares of the family dog revealed MRSA colonization with an indistinguishable PFGE type of MRSA. Further recurrence of MRSA infection and colonization in the couple was only halted after successful eradication of MRSA from the dog [42].

Equine to human transmission of MRSA infection has also been reported in a 24-h-old foal that was admitted to the Ontario Veterinary College Veterinary Teaching Hospital (OVC-VTH) neonatal intensive care unit for treatment of acute renal failure and septicemia. MRSA had been isolated from the admission nasal swabs of both the foal and its mare. MRSA arthritis and omphalophlebitis had developed in the foal during its course of illness. Seven days after admission, three cases of MRSA skin infections of the foal watch personnel were reported, and MRSA colonization was identified in 10 of 103 (9.7%) screened personnel (four foal watch personnel and six veterinary personnel). All isolates were indistinguishable via PFGE and classified as CMRSA-5 [43].

Recent reports suggest that pig farmers are at increased risk of nasal *S. aureus* (including MRSA) colonization. In 2003 Voss et al. demonstrated transmission of MRSA between pigs and pig farmers, pig farmers and their families, and on to a nurse and patient in a nearby hospital where three different MRSA strains were

identified, with an apparent increase in the widespread prevalence of the spa-type t108 strain [44]. In a case–control study done in the Netherlands, 32 out of 35 case patients were carriers of nontypable MRSA (NT-MRSA) and the multilocus sequence typing (MLST) of their isolates was consistent with sequence type (ST) 398. The authors reported that the geographic origin of this NT-MRSA correlated with the density of the pig population, and that the carriage of NT-MRSA was significantly related to contact with pigs and cattle ($P<0.01$) [45]. This study also found that the percentage of NT-MRSA in relation to the overall number of MRSA isolates in the Netherlands had increased from 0% in 2002 to 21% at the end of 2006.

Animal to human transmission of MRSA infection has been reported from major food animals. Lee et al. conducted a study that was designed to determine the prevalence of MRSA isolates among major food animal-related specimens and to determine their genetic relatedness to human MRSA isolates. They found 15 mecA-positive methicillin (oxacillin)-resistant *S. aureus* isolates out of 1913 (3.6%) samples from major food animal-related specimens. Twelve were from dairy cows and three from chicken specimens. Random amplified polymorphic DNA (RAPD) patterns were generated by PCR and showed that six of the isolates from animals were identical to the patterns of the isolates from humans. These data indicated the possibility of transmissions of MRSA infection to humans through contaminated food products made from these animals [38].

On the other hand, there is also evidence that transfer of MRSA strains can occur between humans and animals. Baptiste et al. reported transmission of the predominant human epidemic strain EMRSA-15 between three veterinary staff members and three dogs, suggesting that while interspecies transmission of identical MRSA isolates can happen between pets and humans in contact with them, the original source of the infection and the direction of transmission may be uncertain [46].

6 A Call for an Action

The international public health authorities are urging countries to implement integrated antimicrobial resistance (AMR) surveillance systems. In Canada, The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) was designed to establish a national surveillance system to monitor AMR and antimicrobial use in the agri-food and agriculture sectors and the impact of resistance on human health. It is designed to generate antimicrobial resistance information from “farm to fork,” as well as from human and animal clinical cases [47]. This program is similar to the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP) in Denmark [48], which was established in 1995, and the National Antimicrobial Resistance Monitoring System (NARMS) in the United States [49], which was established in 1996.

All of these programs are designed to monitor the consumption of antimicrobial agents and the occurrence of antimicrobial resistance. They allow for the inves-

tigation of associations between the use of antimicrobial agents in animals and humans and the occurrence of resistance among bacteria from animals, foods, and humans.

On July 3, 2008, the US Food and Drug Administration (FDA) published a final rule that prohibits the extra label use of cephalosporin antimicrobial drugs in food-producing animals, including, but not limited to cattle, swine, chickens, and turkeys [50]. Data provided by the Canadian Animal Health Institute (CAHI) show a dramatic decline of 29% in the amounts of distributed active antimicrobials used for farm and companion animals over a 3-year period, with 1.6 million kg of antimicrobials being distributed in 2001 and 1.1 million in 2003. This decline can be attributed to several factors including the increased awareness of the need for judicious use of medications and improvements in production practices [51].

7 Pets and Immunocompromised Hosts

Immunocompromised patients that are considered at high risk for serious infection from pets include people with waning immunity such as the elderly, children less than 5 years of age, pregnant women, and the clinically immunocompromised. The most recent written evidence-based guidance was produced by the Centers for Disease Control and Prevention (CDC, 2009) for HIV-infected persons and includes the following [6, 52]:

- When obtaining a new pet, HIV-infected persons should avoid animals aged <6 months.
- HIV-infected persons should avoid contact with any animals that have diarrhea.
- HIV-infected pet owners should seek veterinary care for animals with diarrheal illness, and a fecal sample from such animals should be examined for *Cryptosporidium*, *Salmonella*, and *Campylobacter*.
- HIV-infected persons should wash their hands after handling pets, including before eating, and should avoid contact with pets' feces.
- HIV-infected persons should avoid contact with reptiles (e.g., snakes, lizards, iguanas, and turtles) as well as chicks and ducklings because of the risk for salmonellosis.
- Gloves should be used during aquarium cleaning to reduce the risk for infection with *Mycobacterium marinum*.
- Contact with exotic pets (e.g. nonhuman primates) should be avoided.

It may well be prudent to apply such guidelines to other immunocompromised individuals. Pet animal exposure should be avoided in child care facilities and animal exposure should be minimized as much as possible in children less than 5 years of age with the emphasis of proper hand hygiene. The role of pediatricians and veterinarians in pet selection should not be dismissed, and their advice about pet-related hazards and safe pet ownership is important.

8 Conclusion

Humans are usually an accidental host that acquires disease through close contact with an infected animal. Animals are responsible for transmission of an extensive array of zoonotic pathogens that are transmitted by different routes, but this risk of transmission of infections is low and may be further reduced by simple precautions.

Antimicrobial resistance is increasing among organisms causing infections in pets and domestic animals. They are able to acquire and exchange multidrug-resistant pathogens with humans, and this problem has been recognized particularly with respect to MRSA.

Data on pet animals are needed for guiding antimicrobial use policy in small animal veterinary practice and assessing the risk of transmission of antimicrobial resistance to humans. The role of public health in the implementation of quality assurance programs on farm and raising awareness of the need for judicious use of antimicrobial agents will become increasingly important. It is not surprising that since we share our world with animals, we share risks of infections with them too.

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