Global Insights into Antimicrobial Resistance and Antimicrobial Stewardship in Cats and Dogs: Exploring Zoonotic Transmission of Drug Resistant Superbugs to Pet Owners

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Abstract

Cats and dogs have been kept as "family members" in houses since the middle of the 20th century. Pets can still transmit various zoonotic pathogens to people. Because of close interaction between people and their household pets, there is the possibility of zoonotic transmission of antimicrobial multi-drug resistant bacteria like MRSA, MRSI, MRSP, *Enterococcus*, and *Acinetobacter baumannii* to pet owners. The transmission of these drug resistant bacteria to people occurs through direct contact with contaminated food, water, and environment and posing a serious threat to people health. Antimicrobials are frequently prescribed for cats and dogs in veterinary medicine including many of the same antibiotics are also used in human medicine. However, antimicrobial resistance (AMR) is a rising global public health concern in veterinary medicine and human medicine. The concerning resistance genes like *mcr* have been found by researchers in veterinary patient isolates, and there is evidence of resistant pathogens spreading across households. Veterinary antimicrobial stewardship is a relatively new field, despite being well-established in human medicine. However, this chapter highlights the risk factors associated with zoonotic transmission of multi drug-resistant bacteria from cats and dogs to people, also emphasizing the prevention strategies.

Keywords: Zoonosis, Drug resistant bacteria, Antimicrobial resistance, One Health, Pet owners, Veterinarians

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Introduction

A zoonotic bacterial disease is an illness that people and animals can contract quite frequently. About 1500 pathogens have been identified to infect people and sixty-one percent of these cause zoonotic infections. The emergence of zoonotic bacterial pathogens is due to global changes in climate, overuse of antibiotics and closer contact with animals. Recent studies have demonstrated that the risk of zoonotic bacterial pathogens is higher than it has ever been before. It is most likely because of increased interaction with adopted small animals, which are welcomed and treated like family members (Cantas and Suer, 2014).

Now-a-days, companion animals like cats and dogs are frequently considered as family members and plenty of households have close or direct contact with pets on regular basis (Kaspar et al., 2018). Globally, there are about 223 million people who have pets (Hamame et al., 2022). Pet ownership is useful for physical and mental health of people (McNicholas et al., 2005). Likewise, the intimate contact of pets with their owners and the space around them (beds, kitchen, and floors) create risk for people and their pets contracting multidrug-resistant bacteria. In addition to, making it even more difficult to prescribe the patient an effective antibiotic course of treatment, antimicrobial resistance (AMR) can spread to humans and other animals through horizontal genetic material transfer, making the management of other diseases much more complicated (Grakh et al., 2022). As AMR bacteria can spread among animals, humans and the environment, their spread has become a major concern in one health (Velazquez-Meza et al., 2022).

Globally, antimicrobial resistance (AMR) has a significant impact due to overuse and misuse of antibiotics in both human and veterinary medicine. Antimicrobial resistance (AMR) happens when viruses, bacteria, fungi or parasites have the capacity to survive in the presence of antibiotics (Ahmed et al., 2024). A serious issue is the overuse of antibiotics in both human and animal populations, primarily as a result of unchecked quackery practices. Antimicrobials are used to treat various infectious diseases of companion animals (cats and dogs); however, number of bacterial pathogens that are resistant to a number of antibiotic groups are rising steadily (Rodríguez-Rojas et al., 2013; Odoi et al., 2021). Coagulase positive *staphylococci* include methicillin resistant *staphylococci* (MRSA), *Staphylococcus intermedius* (MRSI) and *Staphylococci pseudintermedius* (MRSP), while coagulase negative *staphylococci* and extended spectrum beta lactamase producing *Enterobacteriaceae* can inhabit companion animals and cause infections to people and pets (Kaspar et al., 2018). Pets can transmit *Salmonella* spp. to people through direct contact with feces and handling commercial treats of pets (Murphy et al., 2009).

In companion animals, particularly dogs, the following species of bacterial pathogens warrant the need of antibiotics: *Salmonella*, *Campylobacter*, *Staphylococcus*, *E. coli* and *K. pneumoniae* (Guardabassi et al., 2004; Banerjee et al., 2020). According to a recent investigation, over 83% of broad-spectrum antibiotics and almost 71% of the most important antibiotics for human medicine are used in veterinary practice to treat infections in cats and dogs in European countries (Joosten et al., 2020). This antibiotic usage may favor antimicrobial resistant bacteria, which people and their pets contract frequently (Murphy et al., 2012). Many people have questioned whether using some antibiotics in animals are appropriate due to worries regarding zoonotic transmission of antimicrobial resistance to people. The majority of these concerns are about use of antibiotics in food animals as compared to companion animals. A significant issue in companion animals is antimicrobial resistance (AMR), which has increased the potential of treatment failure, increased the expense of medical treatment for patients and complicated the public health issues (Awosile et al., 2018).

The growing and empirical use of antibiotics has led to the emergence and spread of multidrug resistant bacteria, which impact human and animal health (Shaker et al., 2024). Furthermore, concern is increased over the growth of multidrug resistant bacteria in companion animals since it limits the potential usage of antibiotics to treat infections. The studies that periodically assess antimicrobial resistance (AMR) are crucial for guiding treatment choices and developing innovative strategies because antimicrobial resistance is a dynamic phenomenon (Gómez-Beltrán et al., 2020).

This chapter explores that knowledge regarding antimicrobial resistance (AMR) transmission between pets and their owners is crucial since it can inform policy and point to research or solutions required to use a One Health concept to address antimicrobial resistance (AMR) worldwide.

Pets Borne Zoonosis

Animal bites and scratches are the most important ways that people can contract zoonotic bacterial illnesses. Many of dog breeds such as German sepherd, pitbull, huskies, Rottweiler and chows have been identified to be effective in preventing dog bite assaults. Nearly half of the zoonotic infections in the United States have been caused by pit bulls, about three times greater than German shepherds. There are hundreds of various pathogenic microbes particularly *Pasteurella* sp., which are present in oral cavity of healthy pets. In contrast to 60% of cat bites, only 20% of dog bites lead to an infection. After a cat bite, the risk of contracting *Pasteurella multocida* bacteria is ten times greater than after a dog bite (Cantas and Suer, 2014).

An estimated 20% of human infections occur due to animal bite or scratches (Zambori et al., 2013). It has been discovered that the oral microbiota of pets and bacteria culture from pet bite infections in people are identical. Aerobic microbes such as *Pasteurella multocida* (50%), *Staphylococcus* (46%), alpha-hemolytic *Streptococcus* (46%), *Neisseria* (32%), and *Corynebacterium* (12%), lead to an infection are frequently found in dog bite wounds while anaerobic microbes isolated from infected wounds include *Fusobacterium nucleatum* (16%), *Propionibacterium acnes* (14%), *Prevotella heparinolytica* (14%), *Peptostreptococcus anaerobius*(8%), and *Prevotella intermedia* (8%) (Abrahamian et al., 2011).

It is rare to isolate common human skin microbes or other environmental pathogens from infected bite wound of a person (Abrahamian et al., 2011). Generally, infection develops within 8-24hs after animal bite and the site of injury experiences varying degrees of pain. Following cellulitis, there may be a pus filled discharge that occasionally has fouls smell. After animal bites, people who have weak immune system due to diabetes or other liver problems are often at risk for developing severe infections. In such cases, people may develop bacteremia quickly and die (Zambori et al., 2013). A penetrating bite wound near the joints and bones can lead to septic arthritis and osteomyelitis. The microbial makeup of dental plaque biofilm production in pet's mouth is a crucial component of human wound chronicity (Kirketerp-Møller et al., 2011).

Methicillin Resistant *Staphylococcus* (MRSA) Infection

The frequent human commensal bacterium is *Staphylococcus aureus* which develops resistance to beta-lactam antibiotics by acquiring genes that encode a modified penicillin-binding protein. Methicillin resistant *Staphylococcus* infection (MRSA) frequently exhibits resistance to non-beta lactam antibiotics. Infection and colonization of Methicillin resistant *Staphylococcus* infection (MRSA) were once thought to be a major cause of nosocomial infections, however they are frequently found in people living outside of healthcare centers (Cohn and Middleton, 2010). *Staphylococcus pseudintermedius* is more likely to colonize and infect cats and dogs compared to *Staphylococcus aureus*, although this bacterium can also acquire genes that encode methicillin resistance (MRSP). Diagnosing MRSA and MSRP has consequences for treating infected animals and preventing zoonotic transmission. According to recent findings, household pets may contribute to MRSA transmission (Faires et al., 2009; Weese et al., 2006).

A comprehensive population structure of human isolates from the same lineage was compared to 46 multilocus gene sequences type ST (22) MRSA isolates from dogs and cats in the UK. Phylogenetic analysis suggested a human source for isolates infecting companion animals. It was revealed that all companion animal isolates were distributed throughout the MRSA-15 (EMRSA-15) pandemic clade and arranged with human isolates from the UK. Human isolates were categorized below from isolates of companion animals (Harrison et al., 2014).

According to one study, the majority of Methicillin resistant *Staphylococcus* infection (MRSA) isolates were found resistant to aminoglycosides, B-lactam, second-generation cephalosporins and lincosamides (Stella et al., 2020). However, one study found that MRSA isolates had an intermediate susceptibility to vancomycin. Since vancomycin is used as a last resort to treat Methicillin resistant *Staphylococcus* infection (MRSA) in people. Similarly, a *mec*A gene makes it possible for *staphylococci* to exhibit B-lactam resistance (Hoet et al., 2011; Rojas et al., 2017; Stella et al., 2020).

A new study examined the risk factors and prevalence of MRSA transmission in household pets living with an MRSA infected individual. A swab approach was used to screen 99 pets (52 cats and 47 dogs) living with an MRSA-infected person. This screening was done from 66 houses. Two methods were used to genotype human and pets isolates, and the results were analyzed for concordance. Nine (13.6%) households had eleven (11.5%) pets that tested positive for MRSA, although only six of these houses had genetically concordant strains from human and animal sources. Pet carriage and human infection by strain USA 100 were significantly correlated (Morris et al., 2012).

A significant source of MRSA is unhygienic conditions in environment (Lutz et al., 2013; Rojas et al., 2017). Therefore, decreasing the transmission of MRSA in veterinary hospitals can be achieved by adopting appropriate control measures for infection prevention and screening of animals before hospitalization. This may reduce expenses associated with prolong hospital stays (Shoen et al., 2019; Stella et al., 2020; Loeffler et al., 2010).

Methicillin Resistant *Staphylococcus pseudintermedius* (MRSP) Infection

In companion animals, the major source of opportunistic infection is MRSP (Singh et al., 2013). This bacterium has been found in asymptomatic animals, fomites, implant surgical sites and surroundings of veterinary hospitals (Lutz et al., 2013; Julian et al., 2012). It has been demonstrated that certain veterinary facilities such as floors, tables, chairs and operating rooms contain Methicillin resistant *Staphylococcus pseudintermedius* (MRSP). Additionally, certain Methicillin resistant *Staphylococcus pseudintermedius* (MRSP) infection can withstand disinfection and cleaning (Fungwithaya et al., 2022).

It is known that MRSP is extremely resistant to the antibiotics frequently prescribed to treat *S. pseudintermedius* infections (Marsilio et al., 2018). Like MRSA, MRSP is also capable of acquiring *mec*A gene. It was demonstrated that coagulase negative *staphylococcus epidermidis* is frequently identified in humans can transfer the mecA gene to coagulase positive *staphylococcus pseudintermedius,* which is isolated from dog's skin (Shoen et al., 2019).

The Methicillin resistant *Staphylococcus pseudintermedius* (MSRP) related zoonotic cases are uncommon (Singh et al., 2013). Because of the concerning spike in MRSP cases among pet owners, dogs and veterinary employees, adequate hand washing should be practiced both before and after patient contact as well as after coming into contact with possibly contaminated environmental sites in veterinary hospitals.

Enterococcus Species

Enterococcus species are opportunistic pathogens which are found in intestinal flora of dogs and cats (Boerlin et al., 2001; Ossiprandi et al., 2008). In veterinary medicine, *enterococcus* species have been known for causing hospital acquired infections associated with urinary tract infections (Comerlato et al., 2013). The primary source of transmission is contamination of fomites from feces (Mount et al., 2016).

The two most common species found in dogs are *Enterococcus faecalis* and *E. faecium.* The *E. faecalis* is the most prevalent *enterococci* among the two species. There have also been reports of commensal and pathogenic multi-drug resistant *enterococci* organisms. The overuse and misuses of antibiotics are a major contributing factor for existence of multi-drug resistant among *enterococcus* species (Aksoy et al., 2010; Oh, et al., 2018). It is also feasible that some people have developed resistance through different process such as mutation or gene transfer (Ossiprandi et al., 2008).

The development of vancomycin-resistant *Enterococcus faecium* is concerning because it is a crucial antibiotic used to treat enterococci infections and is mediated by *van*A genes (Argudín et al., 2017; Oh et al., 2018). These genes are crucial because they cause multidrug resistance and can spread to other bacterial species like staphylococcus and making it more difficult to treat hospital acquired infections (Oh et al., 2018). Additionally, these genes may spread to people from animals (Boerlin et al., 2001).

Acinetobacter baumannii

Acinetobacter baumannii is a commonly found opportunistic nosocomial pathogen in severely ill and immunocompromised people (Lee et al., 2007). *Acinetobacter baumannii* in the community may be spread through saliva of diseased pets showing respiratory signs because this bacterium can be spread to people when saliva comes in contact with people, especially, children. Furthermore, isolates of this pathogen from cats and dogs are more similar to human strains, indicating that people may be infecting their pets through close contact (Wareth et al., 2019).

Recent studies have investigated the possible significance of pets as a reservoir for community imposed *Acinetobacter baumannii* infections (Belmonte et al., 2014). According to recent reports, *Acinetobacter baumannii* has been identified in pets, and human cases have been linked to isolates of this bacterium from cats and dogs (Zordan et al., 2011). According to one study, *A. baumannii* was found in 6.5% of oral swabs from diseased pets with respiratory symptoms.

Recently, this bacterium has been recognized as a multi-drug resistant superbug which causes morbidity and mortality in humans (Richards et al., 2015). The development of antimicrobial resistance (AMR) is globally monitored by carbapenem resistance in *Acinatobacter baumannii* (Richet et al., 2001). There is increasing evidence that the carbapenemase gene is a naturally occurring gene that is specific to *Acinetobacter baumannii* (Héritier et al., 2005).

According to recent study, 10 (6.5%) out of 154 diseased pets were detected positive for *Acinetobacter baumannii* infection, where 6 dogs (8.1%) and 4 cats (5%) showed multidrug resistant *Acinetobacter baumannii* (Shaker et al., 2024). Similarly, *Acinetobacter baumannii* isolates from dogs in a South African veterinary university hospital showed a high prevalence of multi-drug resistance (Sebola et al., 2023). Globally, multi drug resistant *A. baumannii* is emerging in veterinary hospitals, and raising concern for public health (van der Kolk et al., 2019). Notably, there was a high prevalence of tetracycline, penicillin, and cephalosporin resistance. This is alarming because these antibiotics are often used to treat eyes, skin, respiratory and reproductive infections of pets (Valiakos et al., 2020).

Zoonotic Transmission and Health Risks Associated with Colistin Resistance (*mcr*) Genes between Pets and Humans

Cats and dogs harbor zoonotic microbes through intimate physical contact with owners (e.g., licking and contact with furnishings), as well as their surrounding areas (carpets) (Faires et al., 2020). The transfer of pathogenic microbes and resistance genes between animals and their owners has been widely observed (Effelsberg et al., 2021; Trung et al., 2017)). Antimicrobial resistance (AMR) genes discovered in hospitalized patients occasionally resembled those found in pets. Vigilance is necessary to prevent the spread of drug resistant microbes between dogs and their owners (Pomba et al., 2020).

The *mcr*-1 and *mcr*-2 colistin resistance genes are highly susceptible to zoonotic transmission, as these genes are more common in animals than in people. (Skov and Monnet, 2016). Pet owners are mainly at risk of acquiring emerging pathogenic organisms in their homes. These people come into contact with bacteria that have the *mcr* gene or bacteria that are naturally resistant to colistin, particularly those associated with human illnesses. Vancomycin-resistant enterococci are naturally colistin-resistant bacteria that can spread from pets to their owners, posing a public health concern (Werner et al., 2013).

Dogs and their owners have been diagnosed with pneumonia and other respiratory illnesses in Egypt, China, and UK. The following colistin-resistant bacteria were linked to the pneumopathy: *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Escherichia coli*, and *Enterobacter hormaechei* harboring *mcr*-1 or *mcr* (Wang et al., 2018; Khalifa et al., 2020; Scott et al., 2019). Multiple antibiotic resistances showed by bacteria are a serious public health concern that can arise when *mcr* genes co-occur with other resistance genes. Colistin-resistant isolates found in owners and their pets may be associated with genes that resist β-lactam antibiotics. According to genome analysis, the following *mcr* genes, specifically *bla*TEM, *bla*CTX-M, and *bla*SHV were associated with B-lactamases (Lei et al., 2017; Rapoport et al., 2016).

Pet Owners and Veterinarian Interactions: Exploring Drivers of Antimicrobial Resistance (AMR)

It has been showed that animals may serve as reservoirs for resistant pathogens, particularly if infections are not adequately and thoroughly treated. Furthermore, veterinary medicine recognizes that intimate physical contact of pets with people is a special and crucial part of antimicrobial resistance in pets (Guardabassi et al., 2004). This may result in a higher risk of resistant bacteria spreading between pets and people (Wieler et al., 2011).

Moreover, there are a lot more pets now, and pet welfare is receiving more attention, which results in a better care for diseased animals and more frequent antibiotics usage for pets. This is especially concerning for antibiotics used in human medicine, particularly those referred to as "last resort" therapies for potentially lethal infections (Guardabassi et al., 2004). Human mortality is expected to rise as a result of increasing resistance particularly to these antibiotics. Antimicrobial resistance (AMR) can rise due to interspecies transmission because of a feedback loop of resistance reservoirs and changing generations of resistant microbes (Figure 1) (Lloyd, 2007; Van Balen et al., 2017).

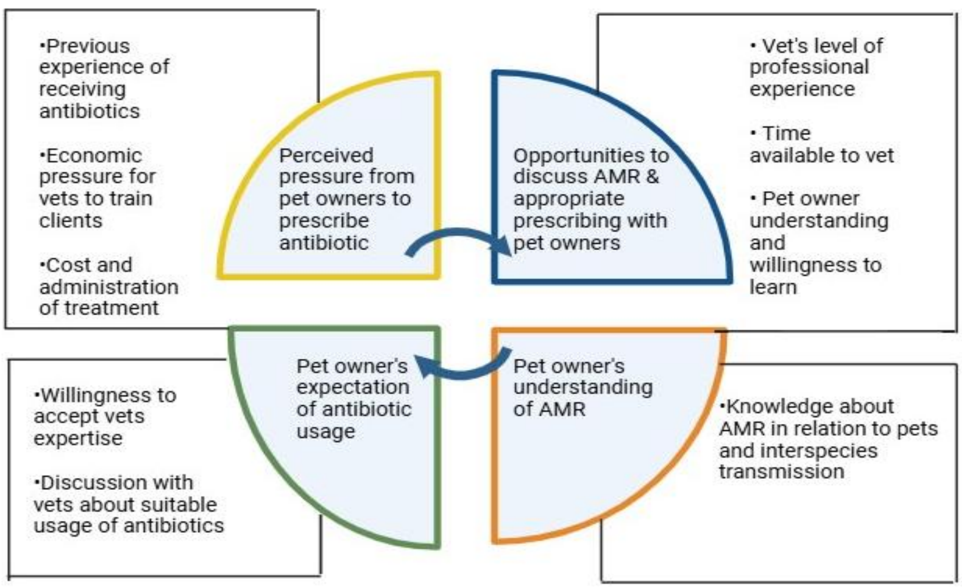

Fig. 1: Factors influencing interactions between veterinarians and pet owners regarding the prescription of antibiotics usage (Smith et al., 2018)

Pet owners and their interactions with prescribing veterinarians are essential to the efficient use of antimicrobials in animal health in order to counteract these drivers of antimicrobial resistance (AMR). Pet owners monitor how their animals are treated; they regulate the use of antibiotics and other behaviors that may directly impact their animal's risk of developing antimicrobial resistance (Lloyd, 2007). Understanding behaviors of pet owners in association with veterinarians could become a crucial component of the global effort to decrease antimicrobial resistance (AMR) in the absence of more potent antibiotics as a solution (Figure 2).

Exploring Antimicrobial Resistance (AMR) and Antimicrobial Stewardship in Veterinary Practice

Because of trends toward a growing number of companion animals and closer pet-human interactions globally, it is crucial to consider the antimicrobial resistance problem from One Health perspective, which seeks to maximize health outcomes by acknowledging the interconnections of humans, animals, plants, and environment (Vercelli et al., 2022). According to studies, pet owners may not fully comprehend how antibiotics are used by their animals and may be reluctant to alter their loving interactions with them (Smith et al., 2018). As a result, veterinarians are crucial to the process of protecting companion animals and their owners from antimicrobial resistance problem through antibiotic stewardship and optimal use. Follow specific guidelines about usage of antibiotics in pets to reduce AMR and zoonotic transmission of drug resistant bacteria (Dickson et al., 2019).

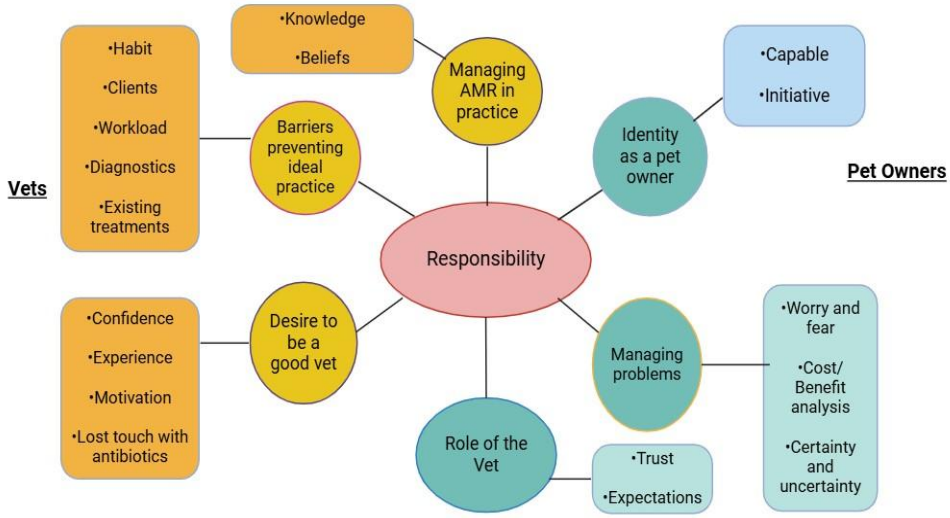

Fig. 2: Thematic map showing views of vets and pet owners regarding antibiotic usage in companion animals (Rhys-Davies and Ogden, 2020)

Globally, several control methods are right now being used in veterinary medicine and human medicine to combat antimicrobial resistance. In small animal clinical practices, antibiotic stewardship program has become more significant. The basic goal of this strategy is to minimize the prescription of unsuitable antibiotics, which generally occurs at the start of empirical treatment without a suitable diagnostic approach. In hospitals and clinics, specific treatment is an effective strategy to prevent the spread of resistance (Vercelli et al., 2021).

There is a need of bacteria colony culturing and susceptible testing of antimicrobials accordingly to limit the resistance variation (Gómez-Beltrán et al., 2020). Information about antimicrobial resistance in companion animals is crucial, as it can guide logical early treatment options, conducting risk assessments of the effects that antimicrobial resistance in bacteria from companion animal has on individuals, and creating public policy and antimicrobial stewardship guidelines (Awosile et al., 2018).

Futures Perspectives and Conclusion

Dog bite injuries in everyday human animal interactions are not unforeseen, particularly for school-age kids. The majority of these bite wounds are not recorded in hospitals and treated by patients themselves by using first aid medications. All bites should be taken seriously, particularly if skin is not intact. Immediate diagnosis and treatment can prevent wound complications. After touching of pets, encourage the owners to wash their hands thoroughly before drinking and eating. Avoid direct mouth to mouth contact with pets. Avoid directly handling the feces of animals by hands to prevent transmission of zoonotic drug resistant bacteria. On a regular basis, nail trimming and oral cavity examination of pets by a veterinarian will decrease bacterial load that people are exposed in case of animal bites or direct contact with pets.

Veterinarians should educate pet owners how to handle diseased, antibiotic treated pets with care due to irreversible consequences of antimicrobial resistance emergence and its spread in family members. Globally, the prevalence of antimicrobial resistance issue in pets is increasing day by day due to inappropriate use of broad spectrum antibiotics by veterinarians. Veterinarian should prescribe an antimicrobial after bacteria culturing. It is important to wash hands thoroughly and wear gloves while handling antibiotics at veterinary clinics. There is an urgent need for smarter antibiotic usage that can help pets recover from potentially fatal diseases. Future efforts to test strategies to decrease the spread of Methicillin resistant *Staphylococcus* (MRSA) infection between pets and humans should be prioritized. Local authorities should develop national veterinarian antimicrobial treatment guidelines based on the most recent periodic surveillance data.

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