Antimicrobial Resistance in Animal Sector

P. Anand Kumar

Contents

Abstract

The antimicrobial resistance (AMR) phenomenon in bacteria is in existence well before the discovery of present-day antibiotics, but the rapidity of its development in bacteria is a cause of great concern as it renders the antibiotics ineffective for therapeutic use in human health and animal health. Antimicrobial use (AMU) is one of the main drivers for AMR in bacteria. The global consumption of antimicrobials in the animal sector is phenomenally increasing at great proportions, especially in low- and middle-income countries. The use of antibiotics as growth promoters in animal feeds for improved animal productivity is a cause of great concern. The AMR is transferrable among bacterial species across the human, animal, and environmental sectors. The AMR in animals has not received much-required attention compared to the human counterparts. As global AMR surveillance network for animals is not available, point prevalence surveys are employed to map AMR in animals. Considerable geographic variation in antibiotic resistance levels is observed in foodborne pathogens, viz., *Escherichia coli*, *Campylobacter* species, non-typhoidal *Salmonella* serotypes, and *Staphylococcus aureus*. Certain

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P. Anand Kumar (✉)
Department of Veterinary Microbiology, NTR College of Veterinary Science, Sri Venkateswara Veterinary University, Gannavaram, Andhra Pradesh, India
e-mail: p_anandkumar@yahoo.com

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classes of antibiotics are listed as critically important in both human medicine and veterinary medicine. Therefore, the rational use of antimicrobials is the need of the hour as antibiotics are indispensable tools in animal health too. In animal sector, the increased AMR is responsible for the financial losses due to higher mortality of animals, reduced productivity, and early culling of breeding and production animals, effecting the livelihoods of livestock and poultry farmers.

Keywords

Antimicrobial resistance (AMR) · Antimicrobial use (AMU) · Point Prevalence Surveys (PPS) · Low-and-middle-income countries (LMICs) · World Health Organization (WHO) · World Organization of Animal Health (WOAH/OIE) · Food and Agriculture Organization (FAO)

1 Introduction

Antimicrobial resistance (AMR) is a fast-evolving phenomenon and a cause of global concern (O'Neill, 2016). World Health Organization (WHO), World Organization of Animal Health (WOAH), Food and Agriculture Organization (FAO), and United Nations Environment Programme (UNEP) are working together as quardipartite to find strategies to mitigate the AMR. The term AMR includes the resistance developed in infectious agents against antibiotics, antiprotozoal, antihelminths, and antivirals. However, in this chapter only the resistance of bacteria against antibiotics in veterinary/animal settings will be reviewed.

The AMR phenomenon in bacteria exists since ancient times, well before the discovery of modern antibiotics. But the great significance that is attached to AMR in the present scenario is due to the rapidity of its development in bacteria, thus rendering the antibiotics ineffective for therapeutic use. Slow and long evolutionary process is responsible for innate AMR, whereas selective pressure due to antimicrobial use (AMU) is responsible for adaptive AMR in bacteria. (Giedraitiene et al., 2011; Perry et al., 2016; Palma et al., 2020). Increased demand for animal protein in human nutrition with intensive livestock farming practices is responsible for increased AMU, which is one of the significant drivers for the development of AMR in animal settings, predominantly in low-and-middle-income countries (LMICs). In humans, antibiotics are used for health, whereas, in animals, antibiotics are used for both health and productivity. The antibiotic growth promoters in animal feeds for improved animal productivity are a cause of great concern (Van Boeckel et al., 2017).

The AMR in animals has not received much-required attention compared with the human counterparts. There is a growing body of evidence that the majority of the infectious diseases of humans are zoonotic in origin (Jones et al., 2008). The AMR is transferrable among bacterial species across the human, animal, and environmental sectors. Therefore, AMR in animals is a double-edged weapon as it may cause untreatable bacterial infections in animals and humans. In LMICs like India, China, Kenya, Uruguay, and Brazil, more resistance is observed in bacteria against commonly used antibiotics in farm animals (Van Boeckel et al., 2019). The quick spread of plasmid-mediated mobilized colistin resistance-1 gene (MCR-1) globally within a short span of its first report in 2014 from a pig farm in China (Wang et al., 2018) further highlighted the urgent need to tackle the AMR issue in the animal sector.

Antibiotic use in animals drives the selection of AMR in animal bacterial pathogens and commensals. Evidence is also growing on antibiotic use in companion and food animals, leading to the spread of antibiotic-resistant bacterial pathogens or their resistant genes to other animals and humans, which makes the treatment of these infections more difficult. In contrast, animals may amplify the antibiotic-resistant bacteria acquired from their owners and act as reservoirs of human infection (Prescott, 2008). *Campylobacter jejuni*, extraintestinal pathogenic *Escherichia coli*, methicillin-resistant *Staphylococcus aureus* (MRSA) or *Staphylococcus pseudintermedius*, vancomycin-resistant enterococci, carbapenemase-producing enterobacteria, and extended-spectrum beta-lactamase (ESBL)-producing Gram-negative bacteria are examples for such infections (Pomba et al., 2017).

Many of the antibiotics used in animals are the same as those used in human medicine, though some of these antibiotics were rejected in human medicine due to toxicity issues (e.g., bacitracin). However, one of these antibiotics (colistin) is now being reclaimed for systemic use in humans. However, documentation of antibiotics use in animals is relatively poor, especially in LMICs (Prescott, 2017). The emergence and spread of antimicrobial (antibiotic) resistance in veterinary medicine/ animal sector arising from the antibiotic use in this sector can be linked to individuals' economic behavior and institutional context (Raboisson et al., 2020).

2 Antimicrobial Use

It was estimated that in 2010 globally 63,151 (±1560) tons of antimicrobials were consumed in food animal production. It is projected to reach 105,596 (±3605) tons by 2030, thus a 67% increase in consumption of antimicrobials is expected in a span of 20 years (Van Boeckel et al., 2015). However, it is interesting to note that the evidence linking the reduced use of antibiotics in food animals to that of AMR in humans is very limited. This suggests more intricate pathways between AMR in food animals and human health (Tang et al., 2017). However, as most classes of antibiotics used for treating the bacterial infections in humans are shared with the veterinary sector, cumulative selective pressure will be exerted on the bacteria, resulting in reduced efficacy of antibiotics-based treatment in both human and veterinary medicine (Aarestrup et al., 2008). The resistance to antibiotics in the animal sector is not only a threat to animals' health, productivity, and welfare but also affects the livelihoods of millions of people who depend on animal husbandry for their income.

3 Antibiotic Growth Promoters (AGPs)

The role of antibiotics in the prevention, control, and treatment of bacterial diseases in animal health is significantly and critically acclaimed. However, unlike in human health, the antibiotics played a different role in animal production as growth promoters in feed for improving the productivity of animals. Appreciable growth enhancement and feed efficiency were observed in animals that are fed AGPs (Teillant & Laxminarayan, 2015). Use of streptomycin in animal feed for growth improvement in chickens was reported by Moore et al. (1946). Improved growth performance in chickens and pigs that were fed chlortetracycline (Aureomycin) further augmented their commercial application in animal feeds (Jukes et al., 1950). The antibiotics have been used at subtherapeutic-level concentrations as AGPs. Swann (1969) raised the possible correlation between the development of antibiotic resistance in bacteria with the use of antibiotics as AGPs in animal feeds.

It was hypothesized that AGPs would have effects on microbiota of the animals and alter their density in favor of improved feed efficiency by improving the absorption in the gut (Gaskins et al., 2002). The AGPs also significantly inhibit the inflammatory responses in the intestine, thus promoting feed absorption and enhancing the growth (Niewold, 2007). Many reports were published on the role of AGPs in improving the feed efficiency and growth rates in animals (Cromwell, 2002). Though the normal microbiota are helpful to the host (animals) in preventing the colonization of pathogenic bacteria, competition for nutrients of the host for maintainability of gut microbiota taxes the costs of nutrition in farm animals (Dibner & Richards, 2005).

Among different classes of antibiotics, ionophores, macrolides, penicillins, and tetracyclines have been mainly used as AGPs in animal feeds, especially in monogastric animals. As the antibiotics are used as AGPs at subtherapeutic concentration levels that are most likely well below the minimum inhibitory concentration (MIC) levels reported for that particular antibiotic, the mode of action of AGPs was doubted many times (Broom, 2017). However, it was reported that the antibiotic naficillin at its sub-MIC values increased the susceptibility of *S. aureus* to phagocytosis in the host (Friedman & Warren, 1974). Antibiotic ampicillin at its sub-MIC values reduced the attachment and colonization (Sandberg et al., 1979), and the antibiotics aztreonam, gentamicin, clindamycin, and trimethoprim at their sub-MIC values reduced the expression of virulent factors in *E. coli* (Hacker et al., 1993). In *Pasteurella multocida,* the antibiotics amoxicillin, chlortetracycline, and enrofloxacin at their sub-MIC values inhibited the growth kinetics and modified protein expression, which were contemplated to increase the antibiotic sensitivity (Nanduri et al., 2006). Research reports are available on the reduced biofilm formation and quorum sensing in certain bacteria on treatment with sub-MIC values of different antibiotics (Cerca et al., 2005; Starner et al., 2008). Furthermore, sub-MIC levels of vancomycin, metronidazole, amoxicillin, clindamycin, cefoxitin, and ceftriaxone were reported to increase the initial lag phase of growth of certain strains of *Clostridium difficile* (Drummond et al., 2003). Similarly, significantly reduced growth rates were observed in *Mannheimia haemolytica* and *Haemophilus somnus* treated with sub-MIC values of chlortetracycline (Reeks et al., 2005).

Perhaps due to all the reasons associated with the use of antibiotics at their subtherapeutic levels such as increased sensitivity of the bacteria to the host immune system and reduced inflammatory response in the intestine to improve gut absorption, etc., antibiotics as AGPs have been extensively used in animal feeds, especially in intensive farming practices. Though over the period it was reported that increased AMU in food animals is one of the chief drivers for increased AMR, there is only a little evidence that AMR originates only from the food animals (Allen & Stanton, 2014; Xiong et al., 2018).

4 Antibiotic Resistance Scenario in the Animal Sector

AMR surveillance is the most significant system to assess the AMR burden in livestock. However, there is no such system for the collection of AMR data in animals at the global level on the lines of WHO's Global Antimicrobial Resistance Surveillance System (GLASS), which estimates the global burden of AMR. Such types of AMR surveillance systems in the animal sector are available in a few European countries, where the AMR data of zoonotic and indicator bacteria in food animals and their products are collected from different age groups of food animal species annually (Magnusson et al., 2021). However, such types of systemic AMR surveillance in animals are not followed especially in LMICs where the antibiotic consumption in the animal sector is high.

In the absence of global AMR surveillance systems in the animal sector, the point prevalence surveys (PPS) were found to be helpful to map the trends in AMR in animals. Identification of indicator bacteria for such surveys is crucial. In the animal sector since the AMR from foods of animal origin is the highest priority for public health, the foodborne bacterial pathogens as indicated by the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) were selected by Van Boeckel et al. (2019) as indicator bacteria in AMR PPS. Therefore, antibiotic resistance in *Escherichia coli*, *Campylobacter* species, non-typhoidal *Salmonella* species, and *Staphylococcus aureus* were studied under PPS to report AMR in animals and foods of animal origin. It was reported that, in LMICs, the rapid increase in AMR from 2000 to 2018 in chickens and pigs is mainly due to increased intensive farming practices adopted for these two species compared to cattle.

Van Boeckel et al. (2019) also reported considerable geographic variation in antibiotic resistance levels. About 56% of pigs and 54% of chickens in the world are found in Asia. Therefore, the largest hotspots of AMR in animals are found in Asia. In regions such as central India and Kenya, where the meat consumption is low and still intensive farming practices have not picked up, the resistance to multiple antibiotics has not yet reached 50%. In the global scenario, the major hotspots for AMR are not found in Africa, except in Johannesburg.

Van Boeckel et al. (2017) reported the highest resistance rates in the antimicrobials such as sulfonamides, tetracyclines, and penicillins, which are commonly used in animal production. Ciprofloxacin and erythromycin have the highest resistance rates of 20–60%, third- and fourth-generation cephalosporins have moderate resistance rates of 10–40%, and linezolid and gentamicin have lower resistance rates of <20% in LMICs. However, different resistance rates were observed for quinolones and aminoglycosides.

When geographic-wise AMR patterns in the foodborne bacterial pathogens were assessed, the quinolone resistance in *E. coli* and *Salmonella* species in LMICs was comparable to the European levels, but the resistance to gentamicin was found to be higher in LMICs. In the United States, the resistance to quinolones was found to be higher than LMICs (Van Boeckel et al., 2019).

The highest rates of colistin resistance (about 18–40%) were found in Asia and the Americas. The research publications on plasmid MCR-1 gene isolated from pigs in China (Liu et al., 2016; Wang et al., 2018) have generated a significant interest in AMR research in the recent past (Sweileh, 2021). As colistin is the last resort for the treatment of infections caused by *Acinetobacter baumannii* and/or *Pseudomonas aeruginosa* in humans, also due to the fast spread of its resistance by horizontal transfer (Sherry & Howden, 2018), the colistin resistance has gained a lot of significance. In the animal sector, the colistin was used not only to treat the infections caused by bacteria of the *Enterobacteriaceae* family but also as a growth promoter (albeit clandestinely) to improve the animal productivity (Davis & Walsh, 2018). The MCR-1 gene was identified in many Gram-negative bacterial species such as *Klebsiella, Salmonella, Shigella*, *E. coli,* and *Enterobacter* in humans and animals (Jeannot et al., 2017). In 2016, the Chinese government banned the use of colistin as a feed additive in livestock and poultry, which was quickly followed by Brazil (Sweileh, 2021). In 2019, the government of India banned the use of colistin in animals. In a study of *E. coli* isolates from humans, animals, foods, and environment, Pormohammad et al. (2019) reported that the prevalence of extended-spectrum beta-lactamase (ESBL)-producing *E. coli* was found to be highest in animals. It is also appropriate to note that Damborg et al. (2009) reported *E. coli* isolates that belong to the same phylogenetic group B2 or D among family members (owners) and dogs (pets).

Restrictions on the use of gentamicin in the animal sector (cattle and poultry) in Europe were found to be directly associated with the lower AMR rates in *E. coli* and *Salmonella* species for gentamicin, whereas significant resistance rates were found for the same in LMICs. In *Campylobacter* species, the highest resistance rate of 60% was found for tetracyclines and quinolones, and moderate resistance rate of <30% was found for erythromycin in LMICs. In the United States, the highest resistance rate for tetracyclines up to 100% was observed. However, the resistance to quinolones in *E. coli* and *Campylobacter* species is lower in the United States compared to the LMICs and Europe due to the ban on the use of quinolones in poultry since 2005 (Van Boeckel et al., 2019).

E. coli is known for its vulnerability to develop AMR against more than one antibiotic that is in circulation for general therapeutic use in humans and animals. It is also a potential reservoir for many AMR genes (Dolejska et al., 2009). Therefore, to monitor the general level of resistance, *E. coli* is considered an excellent indicator. Furthermore, the detection of AMR in commensal bacteria such as *E. coli* will be valuable as it serves as an early warning signal on the development of possible resistance to antibiotics in the pathogenic bacteria (Abbas et al., 2019). Many reports are available on the multidrug-resistant (MDR) *E. coli* in humans, animals, and environment. The potential for transfer of AMR *E. coli* from food animals to humans through the food chain or environment is to be considered with great significance (O'Neill, 2015).

Monitoring AMR in commensal bacteria like *E. coli* from food animals provides significant information on the emergence of AMR and its associated risks to humans (WHO, 2017). Manishimwe et al. (2021) assessed the antibiotic resistance profiles among *E. coli* and *Salmonella* isolated from dairy cattle feces in Texas, USA. A protocol for the detection and estimation of the prevalence of AMR, suitable for resource-limited laboratories in developing countries, was adopted in this study. The non-type-specific *E. coli* and *Salmonella* that were isolated on selective media without antibiotic supplements and the *E. coli* isolates that were not susceptible to third-generation cephalosporins and ciprofloxacin (cultured on selective media supplemented with cefotaxime and ciprofloxacin) were tested for antibiotic sensitivity by disk diffusion test. It was reported that the resistance to tetracycline was found to be the highest among non-type-specific *E. coli* isolated on McConkey agar without antibiotics. Resistance to ceftriaxone is 56.8% in *E. coli* recovered from McConkey agar supplemented with cefotaxime. Resistance to nalidixic acid and ciprofloxacin was 77.3% and 54.5%, respectively, in *E. coli* recovered from McConkey agar supplemented with ciprofloxacin. Manishimwe et al. (2021) further performed whole-genome sequencing on selected bacterial isolates of *E. coli* and *Salmonella* and reported that the phenotypic profiles of antibiotic resistance observed were largely substantiated by genotypic profiles.

Song et al. (2022) assessed the AMR profiles and trends in commensal *E. coli* isolated from the feces of healthy cattle, pigs, and chickens in South Korea during the period 2010 and 2020. A panel of 12 antibiotics, viz. amoxicillin/clavulanic acid, ampicillin, cefoxitin, ceftiofur, chloramphenicol, ciprofloxacin, colistin, gentamicin, nalidixic acid, streptomycin, tetracycline, and trimethoprim/sulfamethoxazole, was used to test the resistance/susceptibility profile of *E. coli* isolates and reported that an overall 56% of tested isolates showed multidrug resistance. The proportion of multidrug-resistant (MDR) *E. coli* was high in chickens (87.1%), followed by pigs (73.7%). However, in cattle, the proportion of MDR isolates of *E. coli* was low (17.1%). Song et al. (2022) concluded that due to such a high resistance in commensal *E. coli* against commonly used antibiotics (including the critically important antibiotics listed), these bacteria could become a potential resistance reservoir and there is a very high possibility to spread this resistance to pathogenic bacteria by gene transfer.

It is commonly perceived that in organized farming antibiotics are misused due to intensive farming systems, which has ultimately become a significant driver for AMR. But reports on MDR *E. coli* even from unorganized pig farms in the Mizoram state of India generate a lot of concern about AMR scourge. Significantly higher resistance against the third-generation cephalosporins was reported in *E. coli* isolates from unorganized piggery farming. The same isolates were reported to exhibit more ESBL and non-ESBL AMR genes, with due correlation to phenotypic observations in antibiotic sensitivity tests. A large number of MDR *E. coli* isolates were reported in unorganized pig farming compared to organized pig farming (Mandakini et al., 2020). This scenario is a serious indication of misuse/improper use of antibiotics and contamination of the environment.

Pseudomonas aeruginosa is regarded as the major human pathogen, and also a significant nosocomial infection. *P. aeruginosa* is also responsible for many diseases in both livestock and companion animals. In cattle, it was reported in mastitis; in horses, it was detected in endometritis; and in dogs, it was recovered from otitis and urinary tract infections (Haenni et al., 2015). The MDR *P. aeruginosa* was isolated mainly from certain otitis cases in dogs. The population of *P. aeruginosa* is generally acknowledged as nonclonal with diversified clonal groups and very little or no association between clonal groups. However, very few reports are available on the studies of genetic diversity and AMR mechanisms in *P. aeruginosa* isolated from animals (Haenni et al., 2015).

In a study conducted by Haenni et al. (2017) to assess the carbapenem resistance in *P. aeruginosa* strains, it was found that certain canine and bovine origins *P. aeruginosa* isolates were not susceptible to imipenem and/or meropenem, though these animals were not treated with the carbapenems at any point in time. The decreased susceptibility was found in meropenem compared with imipenem. Due to mutations in genes coding for efflux pumps, these *P. aeruginosa* isolates showed resistance to carbapenems. These results necessitate the importance of taking up studies on *P. aeruginosa* isolates from animals as there is a high probability that animals may represent a reservoir for MDR *P. aeruginosa* strains.

For another important foodborne pathogen *S. aureus,* the resistance rates were higher across all the antimicrobials in Asia than in other regions. Penicillin, with a 40–80% resistance rate, stood out as the antibiotic with the highest rate of resistance, whereas, for erythromycin, tetracycline, and oxacillin, the resistance rate was 20–60% (Van Boeckel et al., 2019). In *S. aureus*, the sublineages carrying different SCC*mec* cassettes specific to particular geographic regions might have influenced the differences in AMR levels (Asadollahi et al., 2018).

Regarding MRSA, it is interesting to note the evolution of MRSA in livestock from methicillin-susceptible *Staphylococcus aureus* in humans (Price et al., 2012). The livestock-associated (LA-MRSA) clonal complex cc398 is found to frequently infect people both inside and outside of the livestock industry. A predominant human-to-animal direction of transmission is presumed in certain MRSA isolated from dogs and cats because most of these isolates belong to MRSA clonal lineages prevalent in human healthcare facilities. This is a typical case of most likely spillover from “owners (humans)” to “pets (animals)” (Nienhoff et al., 2009).

The MRSA isolated from dairy cows is usually found to be resistant to penicillins and cephalosporins. But isolation of multidrug-resistant MRSA is widely reported (Bhattacharya et al., 2016; Mistry et al., 2016). In such a scenario, if MRSA becomes a common bacterial pathogen of mastitis in dairy animals, veterinarians will be left with few or no antibiotics of choice to treat mastitis (Oliver & Murinda, 2012).

Staphylococcus pseudintermedius is an opportunistic pathogen of dogs that is responsible for skin, ear, and wound infections. The emergence and spread of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) is a classic example of AMR in animal health that has not received the required attention. Pyoderma in dogs due to MRSP was reported for extended treatment periods. However, apprehensions are raised about deeper infections and certain surgical infections with MRSP becoming life-threatening in dogs (Van Duijkeren et al., 2011).

Vancomycin-resistant enterococci (VRE) such as *Enterococcus faecalis* and *Enterococcus faecium* pose challenges in the clinical settings of humans. The emergence of VRE was profoundly observed in European countries, which was attributed due to the widespread use of the antibiotic avoparcin in the 1990s as a growth promoter in animals. Though enterococci are found as commensal bacteria in the intestines of humans and domestic animals, they are also found in the environment. *Enterococcus faecalis* and *Enterococcus faecium* are the most important species recovered from humans and animals (Hammerum, 2012).

Intrinsically enterococci species are resistant to many first-line antibiotics. Varied levels of resistance to cephalosporins and aminoglycosides were reported; furthermore, enterococci can also acquire resistance against quinolones, macrolides, and glycopeptides (Arias & Murray, 2008). Bates et al. (1993) first reported the animal origin of vancomycin-resistant enterococci. Subsequently, several reports were published on the detection of vancomycin-resistant enterococci from different animal species, viz., cats, dogs, horses, pigs, birds, poultry, and foxes, and foods of animal origin like pork and poultry meat (Hammerum, 2012). Though avoparcin was banned as a feed additive for animals between 1995 and 1997 in many European countries, vancomycin-resistant enterococci clones were detected even after 13 years of its ban. This persistence of vancomycin-resistant enterococci might be due to co-selection with other antibiotics and metals (Hammerum, 2012). Extensive typing studies were conducted with pulse field gel electrophoresis (PFGE), amplified fragment length polymorphism (AFLP), and multilocus sequence typing (MLST) for comparing *E. faecium* isolates of animal origin with those of human origin for determining their clonal complex (CC) and sequence types (ST) (Willems et al., 2000).

Different studies were conducted to establish the transfer of vancomycin resistance A (*van*A) gene from *E. faecium* isolate of animal origin to *E. faecium* isolate of human origin. In an experiment, it was found that the transfer of the *vanA* gene was at a high frequency between animal origin and human origin isolates of *E. faecium* (Moubareck et al., 2003). Though based on molecular typing studies, the enterococci are regarded as host-specific or host-adapted that do not necessarily prevent the transfer of AMR genes between animal and human isolates of enterococci. In fact, the AMR genes seem to spread easily between enterococci from different reservoirs (Heuer et al., 2006). It was further reported by Larsen et al. (2011) that similar antibiotic resistance patterns, virulence gene profiles, and MLST/PFGE types were detected in *E. faecalis* isolates from human patients and pigs, thus indicating the significance of pigs with antibiotic-resistant enterococci probably constituting a threat to human health.

Antibiotics use in animals, AMR in the bacteria, and abundance of antibiotic resistance genes (ARGs) in animal manure need to be thoroughly studied to understand the AMR in the animal sector. A larger proportion of antibiotics administered to animals is excreted in the form of parent compound or active metabolites (Van Epps & Blaney, 2016) and contaminates the environment. Ghirardini et al. (2020)

reviewed the reports of antibiotics and their residues in animal wastes during the last four decades and reported higher concentrations of antibiotics like enrofloxacin, oxytetracycline, and chlortetracycline in both untreated and treated manure. Mobile genetic elements (MGEs) such as plasmids and transposons are responsible for AMR spread from manure to soil, thus manure operates as a hot spot for horizontal gene transfer (HGT) of MGE harboring ARGs (Redondo-Salvo et al., 2020). Therefore, the increase in AMR in bacteria of livestock and poultry production systems will have a direct impact on soil health and environment.

5 Point Prevalence Surveys (PPS) to Map AMR

The PPS used to estimate the AMR rates in the animal sector have some limitations. The prevalence of AMR and AMU can be appreciated with PPS at one point in time for human samples in a hospital. But the PPS for animal samples are different as samples from food animals are taken from the healthy animals at the time of their slaughter. The type of microbes and the magnitude of their resistance to antibiotics are different in sick animals compared to healthy animals (Moore, 2019). Therefore, for accurate appreciation of AMR in the animal sector, a global surveillance network system on AMR in the animal sector on the lines of GLASS is the need of the hour. Otherwise, a component may be introduced in GLASS to accommodate the AMR data from the animal/veterinary sector, which will be helpful for integrated assessment of rates of resistance against antimicrobials across the sectors of human, animal, and environment. In India, with support from the FAO, the Indian Network for Fisheries and Animals Antimicrobial Resistance Network (INFAAR) was launched in 2019 by the Indian Council of Agricultural Research (ICAR) with 11 veterinary and animal science institutes and 8 fishery institutes (Mutua et al., 2020).

6 Antibiotics and Animal Health

Antibiotics are indispensable tools in animal health. In animals, antibiotics are prescribed for therapeutic use in conditions like mastitis, endometritis, pyometra, ear infections, systemic bacterial infections, and during surgical procedures (Page & Gautier, 2012). Most of the studies point out the impact of antibiotic resistance in bacterial pathogens of veterinary importance on public health. But the impact of AMR in bacterial pathogens of veterinary importance on animal health has not received the much-needed attention. AMR seriously affects the health and welfare of livestock, food animals, pet animals, and sports animals, which leads to negative social and economic consequences for the farmers and owners (Bengtsson & Greko, 2014). The exact burden of AMR on animal health is still fully not known.

In countries like India where cattle and buffaloes are meant for dairy purpose, mastitis is the condition where most of the time the misuse of antibiotics is noticed (Mutua et al., 2020). In poultry sector, many times farmers trust the representatives of certain companies who provide feed mixtures that contain antibiotic additives under the pretext of improved growth and productivity (Davis & Walsh, 2018).

The WHO has listed certain antibiotics as critically important antimicrobials for human medicine (WHO, 2019). Similarly, the WOAH has also listed certain antibiotics as critically important in veterinary medicine (OIE, 2007). Certain classes of antibiotics are listed as critically important in both the human medicine and veterinary medicine. They include fluoroquinolones and third- and fourth-generation cephalosporins. Therefore, the OIE recommends using these antibiotics with the conditions that (a) they should not be used for metaphylaxis, (b) they should not be used as first-line treatment unless justified and should be guided by antibiotic sensitivity testing, (c) off label use should be limited and reserved when no alternatives are available, and (d) they not to be used as growth promoters.

Infections with MRSA and multi-antibiotic-resistant Gram-negative bacteria in dogs compel veterinarians to explore options for glycopeptides, oxazolidinones, and carbapenems (Papich, 2013). In such situations, veterinarians are perplexed to use such antibiotics keeping in view the emergence of antibiotic resistance in the bacteria with a potential spread to humans. This type of situation has more serious social consequences as these animals are prerequisites for physically and mentally challenged persons to cope with their daily activities (Bengtsson & Greko, 2014). Antibiotic resistance in the animal sector can also have an economic impact on the owner of the animal. For good animal health practices, the availability of effective antibiotics is imperative. However, due to the emergence and spread of AMR, the available arsenal of antibiotics is getting depleted, which will have serious consequences on animal health. In livestock, the increased AMR is responsible for financial losses due to higher mortality of animals, reduced productivity, and early culling of breeding and production animals. This will be eventually responsible for increased prices for foods of animal origin, which will be a burden to consumers (Bengtsson & Greko, 2014).

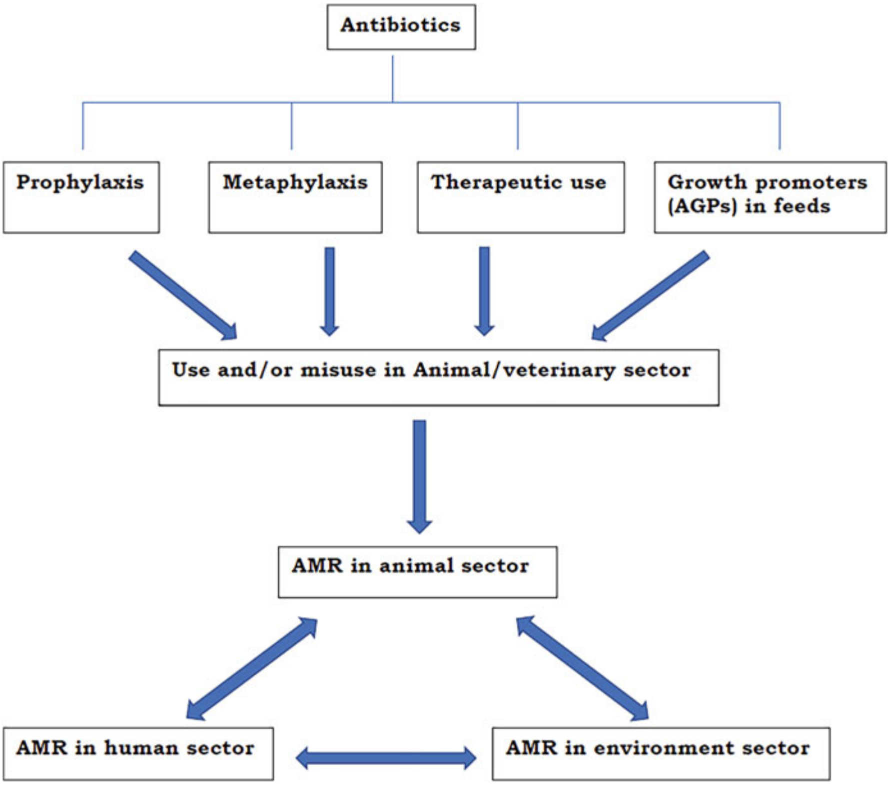
Penicillin was the first choice of antibiotic for mastitis caused by *S. aureus* in dairy animals during the 1950s. However, today penicillin is no longer a first-line therapeutic choice to treat mastitis caused by *S. aureus* (Oliver & Murinda, 2012). Similarly, due to the emergence of resistance against penicillin and tetracycline in *Pasteurella multocida* and *Mannheimia haemolytica,* presently these two antibiotics are not considered as first-line therapeutic choice to treat respiratory infections and pneumonia caused by *P. multocida* and *M. haemolytica* in calves (Portis et al., 2012).

As the older drugs (antibiotics) become obsolete due to the development of resistance, new antibiotics with broad-spectrum activity are introduced for therapeutic use in animal health, which may be responsible for imposing broader selection pressure for developing AMR in the bacteria (Vaarten, 2012).

The World Bank report released in 2017 stated that by 2050 the global livestock population would fall by 3–8% every year due to AMR, with serious consequences on economic and developmental aspects, including sustainable livelihoods. In the event of a high-impact AMR scenario, 11% loss of livestock production is estimated especially in LMICs (Jonas et al., 2017). Therefore, appropriate mitigation measures need to be taken to address the AMR in the animal/veterinary sector.

7 Measures to Mitigate AMR in the Animal Sector

1. Providing effective veterinary services to livestock and poultry sector
2. Medically rational and prudent use of antibiotics by veterinarians
3. Duly implementing the regulatory measures to prevent the sale of antibiotics without prescription
4. Good animal husbandry practices, including improved economical biosecurity settings in livestock and poultry farms
5. Promoting natural products like phytochemicals and essential oils with antimicrobial activity as feed additives to replace antibiotic growth promoters
6. Promoting the use of immunomodulators and synbiotics (probiotics with prebiotics) as feed additives for the overall improvement of animal health and production
7. Vaccination of animals with available vaccines against all the important infectious diseases



Antibiotic Resistance in Animal Sector: An Overview

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