Chapter 2

Necessary Usage of Antibiotics in Animals

Magdy Moheb El-Dein Saad and
Mohamed Bedair M. Ahmed

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.71257

Abstract

Animals could become sick at any time of their lives, just like all people exposed. Many of the antibiotics administered to animals are identical to or closely drugs used in human. All animal species in general and food-producing animals, in particular, are commonly exposed to antibiotics to treat and prevent infectious diseases or to promote growth. Antibiotics would not be necessary if animals were raised differently under good veterinary and husbandry practices that were less crowded and more sanitary. The proper and responsible use of antibiotics in veterinary medicine mandate an active cooperation between all the interested parties involved in livestock production cycles. All parties are invited to act together to ensure the ultimate goals of maintaining the efficacy and safety of veterinary antibiotics and complying the established maximum residue limits (MRLs) of the products of animal origin intended for human consumption. Antibiotics as hazardous substances should be applied and directed during the different steps starting from prescription until ensuring the withdrawal period under the supervision of professionals and veterinarians. Practices indicated that there is a need to improve sensitivity testing services and facilities before prescribing the proper antibiotic.

Keywords: prophylaxis, metaphylaxis, curative, therapy, misuse, resistant bacteria, food-producing animals, drug prescription

1. Introduction

Since the veterinary antibiotic residues and occurrence of bacterial resistance problems had got the attention of scientists and public communities, many questions raised focusing on the main five logics of (5W + 1H) being: What are the alternatives and choices to avoid using veterinary antibiotics? Why we cannot stop usage of antibiotics in food-producing animals? When do veterinary antibiotics are necessary to use? Where do the herd producers get antibiotics for animal use? Who is authorized to prescribe and regulate antibiotics for animal use? And how could antibiotics be effective without any negative effects on public health?

2. Choices and alternatives to control bacterial infections and diseases in companion and food-producing animals

Undoubtedly, animals could become sick at sometime of their lives, just like all people do. Food-producing animals involving large and small ruminants, poultry and aquaculture are often exposed to antibiotics to treat and prevent infectious diseases or to promote growth [1, 2]. Many of the antibiotics administered to animals are identical to or closely resemble drugs used in human [2, 3]. Also, other animal species like pets, dogs, horses and animals used for fur are commonly exposed to bacterial infections during their lives. These groups of animals when showed clinical signs, they could be treated separately [4]. As an example, when clinical symptoms of infections were reported or suspected in horses, dogs and other companion animals, they could be easily monitored with a possible quarantine. So, the risk of the infection spreading in veterinary hospitals and veterinary clinics could be at minimum. The same approach was followed when dogs showed clinical symptoms, they should not be kept with other animals [5, 6]. The issue is completely different when flocks or herds of food-producing animals are exposed to bacterial diseases or infections [7]. The responsibility of antibiotics in veterinary medicine is still the best choice to control and treat bacterial infections. Guidelines on the responsibility and prudent use of antibiotics in animal husbandry were issued by the United Nation Organization of UN-Office International des Epizooties [8] and confirmed by the European Union [6]. The aims of the guidelines are to maintain antibiotic efficacy, avoid dissemination of resistant bacteria and finally, avoid such bacteria to reach human food. Also, the guidelines are addressed to all the interested parties involved in animal husbandry; that is, the veterinary pharmaceutical industry, practitioners, breeders and farmers. The guidelines also exhibited the main role and responsibility of the competent authorities dealing with the production and marketing of veterinary antibiotics. The approved guidelines for the use of antibiotics in veterinary medicine had a set of recommendations and measures acting together to ensure the ultimate goals of: (a) comply with the mandatory standards recommended by the international organizations, (b) maintain the efficacy and safety of antibiotics, (c) prevent or at least reduce transformation of resistant bacteria to human, (d) fulfill and comply the established maximum residue limits (MRLs) of the applied antibiotics and finally, (e) ensure the safety of the products of animal origin intended for human consumption.

3. The prudent and responsible use of antibiotics

The technical committee of UN-Office International des Epizooties [8] recommended the following criteria for the proper and responsible use of antibiotics:

a. Antibiotics as hazardous substances should be applied and technically directed under the supervision of professionals and those have the required experience and skills.

http://dx.doi.org/10.5772/intechopen.71257

b. Antibiotics usage should be applied within the good veterinary practices (GVP) and animal husbandry practices, considering diseases prevention practices like vaccination and improving husbandry conditions.

c. The usage of antibiotics should be limited to their approved and intended use.

d. Where appropriate, testing of isolates from food-producing animals during their production period to adjust therapy.

e. The proper and responsible use of antibiotics in veterinary medicine mandate an active cooperation between all the interested parties involving, administrative and scientific authorities, veterinary pharmaceutical industry, distributors and handlers, veterinary practitioners and livestock breeders and producers.

It is worthy to mention that prudent use of veterinary antibiotics is the most important part of the good veterinary practices (GVP). The first step is commonly dealing with antibiotic prescribing habits. Some practitioners take into account responsible use warnings when antibiotic sensitivity testing is performed. No doubt, those significant differences could be obtained, due to the frequency of sensitivity testing, practitioners skills, background as well as some interfering factors. Practices indicate that there is a need to improve sensitivity testing services and facilities aiming to offer rapid, accurate and cheaper testing before prescribing antibiotics [9]. As more antibiotics are discovered and applied to veterinary clinical use, there is a need to update codes of practices, conduct and ethics. Applying such codes will help to ensure maximizing therapeutic efficacy and minimizing the resistance of microorganisms. Veterinary antibiotics are not only widely used in many countries, if not in all countries to treat and protect animal health, but also they are incorporated into animal feed to improve growth and feed utilization. Regarding antibiotic feed additives, they are poorly absorbed in the gut, so the great portion of such antibiotic additives will take their way into animal secretions such as feces and urine leading to contamination of soil and environment [10–12]. So, the routine use of antibiotics as growth promoters is no longer recommended. Also, veterinarians, practitioners and livestock breeders should have enough knowledge about infectious diseases exposure pathways, fate and effects of veterinary antibiotics, besides the environmental cycle and occurrence.

4. Antibiotic usage in food-producing animals and aquaculture

4.1. Mass production of beef

Raising beef cattle needs relatively little intervention and use of antibiotics comparing with those managed in intensive and feedlots. But commonly beef calves, after weaning aged 6 months and more, are routinely shipped to mass production farms, then maintained in large groups and fed high energy rations. In most developing countries, feedlot animals are kept at high densities which lead to more morbidity, especially in newly received calves. During such production cycle, both pneumonia and diarrhea are the major threat to the herd life. Bovine respiratory diseases have occurred with many causal organisms. These organisms could change during the progression of diseases [13]. Thus, calves are often treated with individual or grouping medication. Consequently, a variety of viral secondary infections contribute to the primary of pneumonia and diarrhea, but treating bacterial infection is still the right medication. Also, the major feedlot health problem of shipping fever complex of pneumonia is an important determinant of antibiotic use. Since beef cattle change ownership more than once during their life cycles, feedlot owners could not easily followed the good veterinary practices. So, the common approach based on the assumption that animals in the group are either susceptible or already carrying diseases [14]. This assumption is applied in USA, when 83% of feedlot cattle received antibiotics through feed or water [15]. The most commonly used oral antibiotics are tylosin, tetracyclines and florfenicols, which could act as prophylactic treatment against liver abscesses, diarrhea, foot rot and respiratory diseases, as well as acting as growth promoters at sub-therapeutic levels [16]. The relation between antibiotic use and resistance in beef cattle appeared wide conflicting results between calves treated with penicillin, streptomycin and tetracyclines and the resistant *Escherichia coli* isolated from their feces [17]. However, in mass production of beef, the fewer antibiotics are used comparing with the other categories of animal production [18].

4.2. Dairy production

As dairy industry is increasing, average herd size and average milk production per head had significantly increased. The common system in most dairy farms depends upon the separation of new-born calves from mothers within a day of birth. The new-born calves are housed separately to control infection and fed milk and/or milk replacers commonly contained tetracycline up to the weaning age 6–8 weeks. To treat or prevent the common diseases of pneumonia and diarrhea, the antibiotics of tetracycline, penicillin and sulfonamides may be administered orally or by injection. Dairy cows are commonly housed at higher densities with great metabolic stress. As milk production increases, parallelly related disease increased, which could negatively affect animal welfare and food quality [19]. Contrary to poultry and beef industry, antibiotics in dairy industry are used for therapeutic functions [20]. Antibiotics are very necessary to treat the common diseases of mastitis, lameness, respiratory diseases and gastrointestinal disorders [21, 22]. In most countries, especially the developing ones, intra-mammary use of antibiotics was frequent, with little if no information, about pharmacokinetics, efficacy and withdrawal period. So, antibiotics use in dairy cattle should be related to the production stage "lactation, dry period and heifers replacement". In lactating dairy cows, mastitis is the most common challenge of diseases. Mastitis caused by intra-mammary infections which could be categorized as clinical or sub-clinical based on clinical signs and some milk composition criteria [23]. To select an appropriate therapeutic protocol, it necessitates enough data about: clinical signs, milk composition and the results of sensitivity testing [24]. Some forms of chronic mastitis like those caused by *Staphylococcus aureus* are poorly respond to antibiotic therapy, but survey studies showed that cephapirin, pirlimycin and amoxicillin were the preferred therapy of clinical mastitis [25]. Because causative organisms of mastitis are classified as environmental, changes in management system could lead to increasing environmental mastitis. However, supportive care and good husbandry practices are recommended for resolution of clinical cases makes antibiotic therapy is not necessary [26]. It is well known that high yielding dairy cows are more susceptible to infectious diseases, especially when transition period of lactation resumes [19]. Good husbandry practices including nutritional support, controlling environmental stress, applying dry cow therapy are the recommended successful criteria for dry period. Dry cow therapy products are available over-counter purchasing. Using teat sealants at dry off represent good option for the prevention of addition intra-mammary infections [27]. Dry cow therapy had positive effect on reducing incidence of mastitis early in lactation without an increase in intra-mammary infection at calving [28]. During the stage of heifers replacement, the selected heifers were fed either on milk replacers with added antibiotics, commonly tetracycline or neomycin, or received whole milk in their home dairy [29]. In general, the primary infections of respiratory diseases and diarrhea necessitate antibiotic therapy in replacement heifers. Diarrhea is the most common cause of mortality in pre-weaned calves commonly treated with ceftiofur, while the primary indication in weaned heifers is respiratory diseases often treated with florfenicols or tilmicosin [27].

4.3. Small ruminants

Sheep and goats are farmed for different products, that is, milk, meat and wool. Sheep and goats necessitate the use of antibiotics to treat the common diseases of mastitis, lameness, respiratory and gastrointestinal disorders [21, 22]. The licensed antibiotics for sheep and goats are very rare, so the use of such drugs depends upon the practitioners experience. Dosage estimation and withdrawal time had not adequately reported for sheep and goats, which increases the risk of residues in human food [30]. The use of antibiotics in small ruminants is relatively low, especially with meat sheep. For therapeutic use, penicillin and tetracyclines are the most common antibiotics, meanwhile tetracycline was more common in feed medication [31]. Usually, small ruminants mastitis is sub-clinical and does not necessarily reduce milk yield and often localized to one udder half. The main adverse effects are related to milk quality and increasing somatic cells counts (SCC) in the yield. It is well established that high SCC are positively related to increase antibiotic residues [32]. Because of the rare antibiotics labeled for small ruminants, mastitis is commonly treated with bovine intra-mammary products, which leads to many adverse effects due to the improper dosage and the estimated withdrawal period [33]. In small ruminants, both broad and narrow spectrum antibiotics can enhance animal performance [31].

4.4. Poultry

Poultry products including eggs and meat are very important sources of animal protein in most developed and developing counties. During the last five decades, broiler chicken production all over the world had increased significantly to meet the increased requirement of animal protein. In Egypt, as an example, poultry industry were grew fast to be highly integrated industry with fewer companies controlling most sources of birds, feed mills, farms, slaughter and processing facilities. Integration of such industry led to standardized management practices including drug treatment practices, especially those related to prevent and control of infection diseases. An intensive production system resulted the spread of pathogens including the zoonotic ones like *Salmonella*. Broiler rations usually contain a coccidiostat, several of which are broader antibiotics of ionophores and sulfonamides. Besides, bacitracin, bambermycin, chlortetracycline, penicillin and virginiamycin are commonly used for growth promotion, feed efficiency in broilers, turkey and egg layers. Also, bacitracin and virginiamycin could be used to control intestinal infections caused by *Clostridium* sp. and/or as growth promoters [34]. Poultry industry necessitates the use of antibiotics at therapeutic and subtherapeutic doses. As gastrointestinal and respiratory diseases represent the common problems challenging poultry industry, coli-bacillosis, necrotic enteritis and *E. coli* are the most causative pathogenic organisms [35]. Survey studies exhibited the common therapeutic use of amoxicillin and tylosin, while lincosamides are used both preventive and curative [36]. Most poultry producers in the developing countries believe well on the use of antibiotics to prevent and curate challenging diseases. In these countries, the use of antibiotics in poultry industry applied without prescription, lacking the necessary information about withdrawal period and the adverse effects to human health and environment [37].

4.5. Fish aquaculture

Antibiotics are very essential additions in fish aquaculture. The ability of antibiotics to control fish diseases is influenced by four main factors: (1) the actual bacterial component, (2) the sensitivity and/or resistance of the bacterial strains to the chosen antibiotic, (3) the proper dosage and treatment intervals and (4) the other contributing stress factors. Antibiotics do not directly cure treated fish, but they are controlling the population growth of a bacteria in a fish which promoting their immune system to eliminate them [38]. Before antibiotics are prescribed to fish and aquaculture, sources of stress involved water quality and temperature, differences between aquaculture species, nutrition and means of antibiotics handling and transportation should be eliminated or at least minimized [39]. Special experience and skills are needed to identify the interfered factors which could be primary or secondary factors affecting bacterial infectious diseases. Such experience and skills besides the sensitivity testing could lead to more efficient treatments and less loss of fish.

5. Persistence development of bacterial resistance threaten human health and environment

Many reports exhibited the variable resistant response of bacterial pathogens [40, 41]. Resistant species of *Salmonella typhimurum* rapidly observed after exposure to certain antibiotics, while *Salmonella duplin* remains sensitive when treated with the same antibiotics. Similarly, *S. aureus* became resistant to penicillin very shortly after administration, meanwhile it needs about 20 years to be observed in *Streptococcus pneumonia* [42]. As bacterial resistance is affected by two main variables of antibiotic category and bacterial species. Resistance to fluoroquinolones in *Campylobacter* sp., apramycin in *E. coli* and *Salmonella* sp. were rapidly observed after drugs administration [43]. Meanwhile, resistance to ampicillin needs to develop more gradually [44]. Similarly, tetracycline and avoparcin persistence are widely affected by many interfered factors including the re-exposure withdrawn antibiotics [42, 45]. The medical impact of previous antibiotic usage in food-producing animals on human health received little attention except for Salmonella and *E. coli*. ***E. coli*** may acquire resistance from the gut micro-flora of the food animal even if the antibiotic is used as a growth promoter [46]. When livestock flocks treated with sulfonamides, amino glycosides or tetracyclines, widespread resistance of bacteria was observed. While the corresponding resistances to other antibiotics like ampicillin and olaquindox is less widespread [44]. It is worthy to mention that multiple resistances to more than one class of antibiotics seemed to be common with animal strains of *E. coli*. ***Salmonella* sp**. showed wide variation between different isolates. The monitoring programs showed that *Salmonella typhimurium* isolates are more resistant to tetracyclines, sulfonamides and streptomycin comparing with the isolates of *Salmonella dublin* and *Salmonella enteritidis* [40]. ***Campylobacter* sp**. had often showed erythromycin resistance, in particular to the isolates of *E. coli* [2]. Enteric *Campylobacter* are rarely requiring treatments, but they showed more tetracycline resistance in human than poultry isolates. Also, isolates of *Campylobacter* obtained from pig exhibited more macroloide and streptomycin resistance comparing with human and poultry isolates [47]. *Enterococci* as *Campylobacter*, both are enteric bacteria in animals. Monitoring programs revealed that pigs and poultry fed avoparcin develop vancomycin resistant *Enterococci* in human. Resistance had been reported in Enterococcal strains obtained from animals to the macroloide lincosamide-streptogramin group including the common antibiotic of tylosin [48]. Resistant non-enteric bacteria were also commonly reported in respiratory tract pathogens in all livestocks and resistant *Staphylococci* from bovine mastitis and small animal infections [49].

6. Cautions and precautions before prescribing veterinary antibiotics

When it is necessary to use veterinary antibiotics to safeguard animal health, many precautions should be considered:

a. The prescription should be based on clinical diagnosis by qualified veterinarian and conducting sensitivity testing to choose the proper antibiotic [39].

b. In general, metaphylaxis antibiotics should never be used, when good veterinary and husbandry practices are available [50].

c. Metaphylaxis antibiotics, when it is necessary, should be prescribed on the basis of clinical findings about the progress of a disease in certain herd or flock [19].

d. It is much better to isolate and separate sick animals and treated them individually [6].

e. Livestock producers should keep files and records to register causes and nature of infections and the available antibiotic products to facilitate the right and correct decision [14].

f. Narrow-spectrum antibiotics could be the first choice, unless sensitivity testing exhibit that they could be ineffective. Contrary, the broad-spectrum antibiotics should be avoided [6].

g. In re-current infection cases, tracing the causal bacteria is recommended to determine why the disease is recurring and to facilitate the pathogenic microorganisms eradication [9].

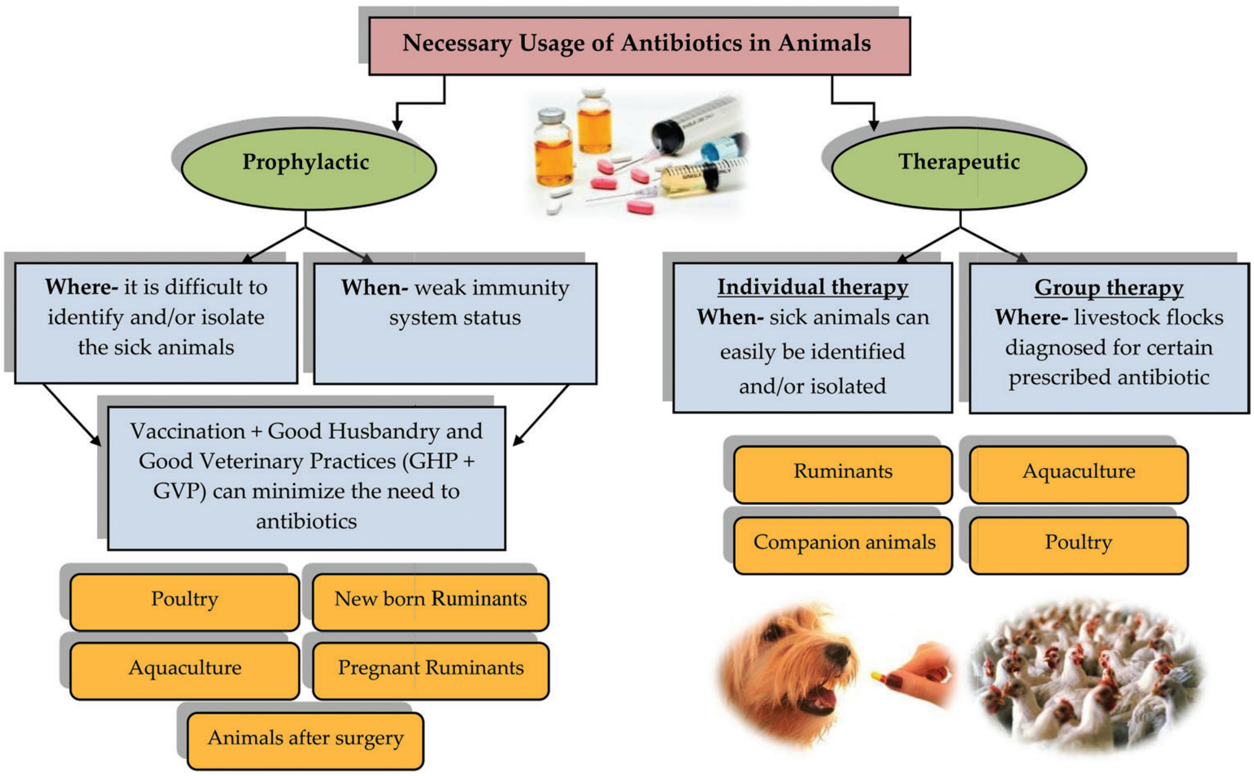

Figure 1. Cases necessitate the use of antibiotics in animals.

h. The need for antibiotic therapy should be reassessed on scientific basis to avoid unnecessary medications.

i. Antibiotics should be administered as the instructions of the prescriber and the manufacturer of the drug [13].

j. All alternative programs to control diseases like vaccination, good veterinary and husbandry practices should be applied together to minimize or reduce the need to veterinary antibiotics [7].

k. Advanced laboratories are recommended to perform rapid and accurate sensitivity testing and more advanced once are required to evaluate and control zoonotic and commensal microorganisms [9].

The common cases necessitate the usage of antibiotics in animals were summarized in **Figure 1**.

7. Economic considerations

It is well agreed and understood that agriculture is practiced to return profit to the farmers and livestock producers. So, two main economic considerations influence the selected programs adopted by livestock producers. The first limiting factor is to select and elect individuals or animal flocks capable to challenge diseases, and the second one is the response of elected animals to enhance most production parameters. It is more economical to prevent diseases than treating them. The preventive efforts involve variety of practices including, proper nutrition, immunization, good veterinary and husbandry practices [4]. Prevention is needed for many diseases and it will be necessary to use prophylactic antibiotics during certain critical periods of animal life. Referring to the second consideration aiming to the response to enhancing most production parameters, livestock producer has the option to do or do not using antibiotics [39]. An economic evaluation of antibiotic usage in animal agriculture is calculated on the basis of return on such use which is not easy to quantify when used as prophylaxis. When antibiotics are used to treat diseases, it is easy to quantify the return, because the cost represents a portion of the necessary total expenses. In both cases, many factors should be considered, that is, costs of diagnosis, culture and sensitivity testing, confirmatory tests and the estimated loss of production based on the affected animals. Actually, the economic return on the use of antibiotics for prevention could be determined by direct comparison with similar farms not using antibiotics. Sub-therapeutic antibiotics are commonly administered to protect animal populations during the critical time when they are susceptible or expose to specific infections and hazards [9]. Thus, such approaches could be considered as economically cost effective, since they reduce the necessity of using higher therapeutic levels of antibiotics.

8. Risk and impact of veterinary antibiotics on human health and environment

Recently, there is a great concern between public in general and scientific communities, in particular, that exposure to pharmaceuticals including antibiotics may have negative effects on both human health and environment [3]. The adverse effects on human health may include the risk of chemical poisoning [51, 52], hypersensitivity reaction, especially with penicillin [53, 54], liver injuries [55], disruption in the normal intestinal flora [56] and occurrence of antibiotic resistance [54, 57]. The adverse effects of exposure to veterinary antibiotic residues in food is very difficult to trace, because bacterial resistance could take very long period of time. For example, the antibiotic chloramphenicol which used in human medicine to treat severe illness, when used as veterinary medicine for food-producing animals, dramatic effects were observed. Thus US-FDA banned the use of chloramphenicol in food-producing animals; even they approved the utility of the drug in treating systemic infections in cattle [9]. Also, because there is no threshold predicted for human aplastic anemia, chloramphenicol is completely banned for use in food-producing animals in many countries including Australia, Canada, EU and USA [7]. It is worthy to mention that chloramphenicol can be synthesized in soil which could be reached to feedstuffs consequently to the edible tissues of the animals. The Codex Committee on veterinary residues had recommended certain criteria for risk assessment of chloramphenicol or any antibiotic when used in food-producing animals [9]. Such criteria evaluate the potential of both short and long term of dietary exposure to antibiotic(s) residues on human health. However, misuse of antibiotics in animal husbandry and aquaculture could lead to the presence of residues in human food [57].

Transformation of antibiotic residues could easily reach soil, surface and ground water via many routes such as sub-surface flow, drain flow or leaching [11, 58]. The concentration of the transformed residues are affected by many factors including the chemical and physical properties of the antibiotic molecule, sorption behavior and persistence, exchange capacity of the soil matrix besides the various climate conditions [16]. Recent reports showed that sulfonamides and chloramphenicol could easily reach ground water, while fluoroquinolones could not leach. The reports added that in most areas of intensive livestock breeding, the source of contamination mainly attributed to irrigation with sewage [12, 16]. The uptake and accumulation of antibiotics into edible plants is commonly initiated when expose to contaminated soil with considerable concentrations of the drugs over time as confirmed by several studies [59–63]. However significant amounts of antibiotics and/or their degraded metabolites are introduced to agro-system via irrigation, fertilization with antibiotic-polluted manures, bio-solids, sludge, sediments and contaminated water [16, 64]. Accumulation and transport of antibiotics to edible plants poses high risk to crops, soil and water ecosystems [63, 65, 66], consequently, increasing risk to both human health and environment [3]. Applying and implementing good veterinary and husbandry practices are most urgent issues to control and reduce both the problems of antibiotic residue contamination and persistence of resistant bacteria.

Author details

Magdy Moheb El-Dein Saad and Mohamed Bedair M. Ahmed*

*Address all correspondence to: m.bedair.nrc@gmail.com; md.bedair@nrc.sci.eg

Department of Food Toxins and Contaminants, National Research Centre, Cairo, Egypt

References

[1] Ungemach FR. Figures on quantities of antibacterials used for different purposes in the EU countries and interpretation. Acta Veterinaria Scandinavica. 2000;**93**(Suppl):89-103

[2] Teuber M. Veterinary use and antibiotic resistance. Current Opinion in Microbiology. 2001;**4**(5):493-499

[3] Saad MM. The risk of human exposure to antibiotic residues from food of both animal and plant origin. European Journal of Biomedical and Pharmaceutical Sciences. 2016;**3**(5):12-15

[4] Gustafson RH, Bowen RE. Antibiotic use in animal agriculture. Journal of Applied Microbiology. 1997;**83**(5):531-541

[5] DSAVA, Danish Small Animal Veterinary Association. Antibiotic Use Guidelines for Companion Animal Practice. 2012. 2015. ISBN 978-87-870703-0-0. Available from: http://www.ddd.dk/sektioner/hundkatsmaedyr/antibiotikavejledning/Documents/AntibioticGuidelines.pdf. [Accessed: July 8, 2017]

[6] EU. Commission Notice No. 2015/C 299/04. Guidelines for the prudent use of antimicrobials in veterinary medicine. Official Journal of the European Union. 2015;**C 299**:7-29

[7] CVO, The College of Veterinarians of Ontario. Use of antimicrobial pharmaceuticals in food producing animals. A Review Report; July 2014:1-30. Available from: https://cvo.org/CVO/media/College-of-Veterinarians-of-Ontario/Resources%20and%20Publications/Reports/GF2BackgroundReview.pdf Accessed: June 12, 2017

[8] OIE. OIE Global Conference on the Responsible and Prudent Use of Antimicrobial Agents for Animals: International Solidarity to Fight Against Antimicrobial Resistance. Paris. March 13-15, 2013. 2013. Available from: http://www.oie.int/eng/A_AMR2013/Recommendations.htm. [Accessed July 1, 2017]

[9] FDA. Summary Report on Antimicrobials Sold or Distributed for Use in Food Producing Animals. Food and Drug Administration, Dept. of Health and Human Services; 2013. p. 1-57. Available from: https://www.fda.gov/downloads/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/UCM440584.pdf. [Accessed: July 1, 2017]

[10] Spaepen KR, Van Leemput LJ, Wislocki PG, Verschueren C. A uniform procedure to estimate the predicted environmental concentration of the residues of veterinary medicines in soil. Environmental Toxicology and Chemistry. 1997;**16**(9):1977-1982

[11] Kim KR, Owens G, Kwon SI, So KH, Lee DB, Ok YS. Occurrence and environmental fate of veterinary antibiotics in the terrestrial environment. Water, Air, Soil Pollution. 2011;**214**:163-174

[12] Ok YS, Kim SC, Kim KR, Lee SS, Moon DH, Lim KJ, Sung JK, Hur SO, Yang JE. Monitoring of selected veterinary antibiotics in environmental compartments near a composting facility in Gangwon Province, Korea. Environmental Monitoring and Assessment. 2011;**174**:693-701

[13] Stanton AL, Kelton DF, LeBlanc SJ, Millman ST, Wormuth J, Dingwell RT, Leslie KE. The effect of treatment with long-acting antibiotic at postweaning movement on respiratory disease and on growth in commercial dairy calves. Journal of Dairy Science. 2010;**93**(2):574-581

[14] Gonzalez-Martin JV, Elvira L, Lopez MC, Villalobos NP, Lopez-Guerrero EC, Astiz S. Reducing antibiotic use: Selective metaphylaxis with florfenicol in commercial feedlots. Livestock Science. 2011;**141**(2):173-181

[15] Carson CA. Canadian beef cattle antimicrobial use and associations with antimicrobial resistance in fecal *Escherichia coli*. [PhD dissertation]. Guelph: University of Guelph; 2010

[16] Kim HB, Borewicz K, White BA, Singer RS, Sreevatsan S, Tu ZJ, Isaacson RE. Microbial shifts in the swine distal gut in response to the treatment with antimicrobial growth promoter, tylosin. Proceedings of the National Academy of Sciences. 2012;**109**(38):15485-15490

[17] Gibbons JF, Boland F, Buckley JF, Butler F, Egan J, Fanning S, Markey BK, Leonard FC. Patterns of antimicrobial resistance in pathogenic *Escherichia coli* isolates from cases of calf enteritis during the spring-calving season. Veterinary microbiology. 2014;**170**(1):73-80

[18] FAO. Antibiotics in farm animal production – Public Health and Animal Welfare. A Report on November 2011. Available from: http://www.fao.org/fileadmin/user_upload/animalwelfare/antibiotics_in_animal_farming.pdf. 2011 [Accessed June 11, 2017]

[19] Trevisi E, Zecconi A, Cogrossi S, Razzuoli E, Grossi P, Amadori M. Strategies for reduced antibiotic usage in dairy cattle farms. Research in Veterinary Science. 2014;**96**(2):229-233

[20] LeBlanc SJ, Lissemore KD, Kelton DF, Duffield TF, Leslie KE. Major advances in disease prevention in dairy cattle. Journal of Dairy Science. 2006;**89**(4):1267-1279

[21] Sawant AA, Sordillo LM, Jayarao BM. A survey on antibiotic usage in dairy herds in Pennsylvania. Journal of Dairy Science. 2005;**88**(8):2991-2999

[22] Avery BP, Rajić A, McFall M, Reid-Smith RJ, Deckert AE, Irwin RJ, McEwen SA. Antimicrobial use in the Alberta sheep industry. Canadian Journal of Veterinary Research. 2008;**72**(2):137-142

[23] Barlow J. Mastitis therapy and antimicrobial susceptibility: A multispecies review with a focus on antibiotic treatment of mastitis in dairy cattle. Journal of Mammary Gland Biology and Neoplasia. 2011;**16**(4):383-407

[24] CVMA. Antimicrobial Prudent Use Guidelines 2008 for Beef Cattle, Dairy Cattle, Poultry and Swine. 2008. Available from: http://canadianveterinarians.net/documents/cvma-antimicrobial-prudent-use-guidelines-2008-for-beef-dairy-poultry-swine. [Accessed: May 30, 2014]

[25] Pol M, Ruegg PL. Treatment practices and quantification of antimicrobial drug usage in conventional and organic dairy farms in Wisconsin. Journal of Dairy Science. 2007;**90**(1):249-261

[26] Roberson JR. Establishing treatment protocols for clinical mastitis. Veterinary Clinics of North America. Food Animal Practice. 2003;**19**(1):223-234

[27] Raymond MJ, Wohrle RD, Call DR. Assessment and promotion of judicious antibiotic use on dairy farms in Washington State. Journal of Dairy Science. 2006;**89**(8):3228-3240

[28] Cameron M, McKenna SL, MacDonald KA, Dohoo IR, Roy JP, Keefe GP. Evaluation of selective dry cow treatment following on-farm culture: risk of postcalving intramammary infection and clinical mastitis in the subsequent lactation. Journal of Dairy Science. 2014;**97**(1):270-284

[29] Walker WL, Epperson WB, Wittum TE, Lord LK, Rajala-Schultz PJ, Lakritz J. Characteristics of dairy calf ranches: Morbidity, mortality, antibiotic use practices, and biosecurity and biocontainment practices. Journal of Dairy Science. 2012;**95**(4):2204-2214

[30] Pengov A, Kirbis A. Risks of antibiotic residues in milk following intramammary and intramuscular treatments in dairy sheep. Analytica Chimica Acta. 2009;**637**(1):13-17

[31] Moon CS, Berke O, Avery BP, McEwen SA, Reid-Smith RJ, Scott L, Menzies P. Rates and determinants of antimicrobial use, including extra-label, on Ontario sheep farms. Canadian Journal of Veterinary Research. 2011;**75**(1):1-10

[32] Gonzalo C, Carriedo JA, García-Jimeno MC, Pérez-Bilbao M, De la Fuente LF. Factors influencing variation of bulk milk antibiotic residue occurrence, somatic cell count, and total bacterial count in dairy sheep flocks. Journal of Dairy Science. 2010;**93**(4):1587-1595

[33] Mavrogianni VS, Menzies PI, Fragkou IA, Fthenakis GC. Principles of mastitis treatment in sheep and goats. Veterinary Clinics of North America: Food Animal Practice. 2011;**27**(1):115-120

[34] Ahmed AM, Gareib MM. Detection of some antibiotics residues in chicken meat and chicken luncheon. Egyptian Journal of Chemistry and Environmental Health. 2016; **2**(2):315-323

[35] Geier MS, Mikkelsen LL, Torok VA, Allison GE, Olnood CG, Boulianne M, Hughes RJ, Choct M. Comparison of alternatives to in-feed antimicrobials for the prevention of clinical necrotic enteritis. Journal of Applied Microbiology. 2010;**109**(4):1329-1338

[36] Hughes L, Hermans P, Morgan K. Risk factors for the use of prescription antibiotics on UK broiler farms. Journal of Antimicrobial Chemotherapy. 2008;**61**(4):947-952

[37] Sirdar MM, Picard J, Bisschop S, Gummow B. A questionnaire survey of poultry layer farmers in Khartoum State, Sudan, to study their antimicrobial awareness and usage patterns. Onderstepoort Journal of Veterinary Research. 2012;**79**(1):1-8

[38] Castro SBR, Leal CAG, Freire FR, Carvalho DA, Oliveira DF, Figueiredo HCP. Antibacterial activity of plant extracts from Brazil against fish pathogenic bacteria. Brazilian Journal of Microbiology. 2008;**39**(4):756-760

[39] De Briyne N, Atkinson J, Pokludová L, Borriello SP, Price S. Factors influencing antibiotic prescribing habits and use of sensitivity testing amongst veterinarians in Europe. The Veterinary Record. 2013;**173**(19):475-488

[40] MAFF, Ministry of Agriculture, Forestry and Fisheries of Japan. A Review of Antimicrobial Resistance in the Food Chain. A Technical Report for the UK Ministry of Agriculture, Food and Fisheries. MAFF Publications, London: 171. July 1998

[41] Bager F, Aarestrup FM, Madsen M, Wegener HC. Glycopeptide resistance in *Enterococcus faecium* from broilers and pigs following discontinued use of avoparcin. Microbial Drug Resistance. 1999;**5**(1):53-56

[42] Jacobs-Reitsma WF, Kan CA, Bolder NNI. The induction of quinolone resistant *Campylobacter* bacteria in broilers by quinolone treatment. Letters in Applied Microbiology. 1994;**19**:228-231

[43] Wray C, Hedges RW, Shannon KP, Bradley DE. Apramycin and gentamicin resistance in *Escherichia coli* and salmonellas isolated from farm animals. Epidemiology and Infection. 1986;**97**(3):445-456

[44] Linton AH, Hedges AJ, Bennett PM. Monitoring for the development of antimicrobial resistance during the use of olaquindox as feed additive on commercial pig farms. Journal of Applied Microbiology. 1988;**64**(4):311-327

[45] Salyers AA, Amabile-Cuevas CF. Why are antibiotic genes so resistant to elimination? Antimicrobial Agents and Chemotherapy. 1997;**41**(11):2321-2325

[46] Chowdhury R, Haque MN, Islam KMS, Khaleduzzaman ABM. A review on antibiotics in an animal feed. Bangladesh. Journal of Animal Science. 2009;**38**(1-2):22-32

[47] Aarestrup FM, Nielsen EM, Madsen M, Engberg J. Antimicrobial susceptibility patterns of thermophilic *Campylobacter* spp. from humans, pigs, cattle, and broilers in Denmark. Antimicrobial Agents and Chemotherapy. 1997;**41**(10):2244-2250

[48] Hammerum AM, Jensen LB, Aarestrup FM. Detection of the satA gene and transferability of virginiamycin resistance in *Enterococcus faecium* from food-animals. FEMS Microbiology Letters. 1998;**168**(1):145-151

[49] Piriz S, Valle J, Mateos EM, Cid D, Ruiz-Santaquiteria JA, Vadillo S. In vitro activity of fifteen antimicrobial agents against methicillin-resistant and methicillin-susceptible *Staphylococcus intermedius*. Journal of Veterinary Pharmacology and Therapeutics. 1996;**19**(2):118-123

[50] Alvarez-Fernández E, Alonso-Calleja C, García-Fernández C, Capita R. Prevalence and antimicrobial resistance of *Salmonella serotypes* isolated from poultry in Spain: Comparison between 1993 and 2006. International Journal of Food Microbiology. 2012;**153**(3):281-287

[51] Donoghue DJ. Antibiotic residues in poultry tissues and eggs: Human health concerns? Poultry Science. 2003;**82**(4):618-621

[52] Ferguson J, Baxtera A, Youngb P, Kennedyb G, Elliottb C, Weigelc S, Gatermannc R, Ashwind H, Steadd S, Sharmand M. Detection of chloramphenicol and chloramphenicol glucuronide residues in poultry muscle, honey, prawn and milk using a surface plasmon resonance biosensor and Qflex® kit chloramphenicol. Analytica Chimica Acta. 2005;**529**:109-113

[53] Riedl MA, Casillas AM. Adverse drug reactions: Types and treatment options. American Family Physician. 2003;**68**:1781-1790

[54] Samanidou V, Nisyriou S. Multi-residue methods for confirmatory determination of antibiotics in milk. Journal of Separation Science. 2008;**31**:2068-2090

[55] Darwish WS, Eldaly EA, El-Abbasy MT, Ikenaka Y, Nakayama S, Ishizuka M. Antibiotic residues in food: The African scenario. Japanese Journal of Veterinary Research. 2013; **61**(Suppl):S13-S22

[56] Cotter PD, Stanton C, Ross RP, Hill C. The impact of antibiotics on the gut microbiota as revealed by high throughput DNA sequencing. Discovery Medicine. 2012;**13**:193-199

[57] Beyene T, Tesega B. Rational veterinary drug use: Its significance in public health. Journal of Veterinary Medicine and Animal Health. 2014;**6**:302-308

[58] Botelho RG, Monteiro SH, Tornisielo VL. Veterinary antibiotics in the environment. In: Emerging Pollutants in the Environment-Current and Further Implications. InTech; 2015. InTech publisher, Rijeka, Croatia-EU. Available from: http://dx.doi.org/10.5772/60847

[59] Kumar K, Gupta SC, Baidoo SK, Chander Y, Rosen CJ. Antibiotic uptake by plants from soil fertilized with animal manure. Journal of Environmental Quality. 2005;**34**:2082-2085

[60] Boxall ABA, Johnson P, Smith EJ, Sinclair CJ, Stutt E, Levy LS. Uptake of veterinary medicines from soils into plants. Journal of Agricultural and Food Chemistry. 2006; **54**:2288-2297

[61] Dolliver H, Kumar K, Gupta S. Sulfamethazine uptake by plants from manure-amended soil. Journal of Environmental Quality. 2007;**36**:1224-1230

[62] Rajapaksha AU, Vithanage M, Lim JE, Ahmed MBM, Zhang M, Lee SS, Ok YS. Invasive plant-derived biochar inhibits sulfamethazine uptake by lettuce in soil. Chemosphere. 2014;**111**:500-504

[63] Ahmed MBM, Rajapaksha AU, Lim JE, Vu NT, Kim IS, Kang HM, Lee SS, Ok YS. Distribution and accumulative pattern of tetracyclines and sulfonamides in edible vegetables of cucumber, tomato, and lettuce. Journal of Agricultural and Food Chemistry. 2015;**63**(2):398-405

[64] Lianfeng D, Wenke L. Occurrence, fate, and ecotoxicity of antibiotics in agro-ecosystems. A review. Agronomy for Sustainable Development. 2012;**32**(2):309-327

[65] Costanzo SD, Murby J, Bates J. Ecosystem response to antibiotics entering the aquatic environment. Marine Pollution Bulletin. 2005;**51**:218-223

[66] Jalal KCA, John BA, Kamaruzzaman BY, Kathiresan K. In: Pana M, editor. Emergence of Antibiotic Resistant Bacteria from Coastal Environment – A Review, Antibiotic Resistant Bacteria – A Continuous Challenge in the New Millennium. InTech; 2012 ISBN: 978-953-51-0472-8. InTech publisher, Rijeka, Croatia-EU. Available from: http://www.intechopen.com/books/antibiotic-resistant-bacteria-a-continuous-challenge-in-the-newmillennium/emergence-of-antibiotic-resistant-bacteria-from-coastal-environment-a-review