Literature Review on usage of veterinary drugs on Antimicrobial Resistance (AMR)

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Abstract

The rational use of veterinarian drugs is essential to fight antimicrobial resistance as a growing threat. This practice includes drug administration based on a precise diagnosis through complementary diagnostic tests, the adequate selection of these, the right dosage, length of treatment, and the compliance with withdrawal and resting periods.

Antimicrobial resistance has become a worldwide health problem due to the indiscriminate use of antimicrobials in animals creating resistant bacteria and spreading it to humans, the environment among others. The mindful use of antimicrobials in veterinary medicine aims to reduce unnecessary usage and promote disease prevention through vaccination and biosafety measures. Furthermore, laboratory tests are recommended to determine bacteria susceptibility to select the most effective antimicrobial.

Healthcare professionals performing within veterinary medicine have a vital role in educating producers and pet owners, increasing the application of measures and alternative options whenever possible. The articulated efforts among said professionals, manufacturers, regulators and pharmaceutical industry is essential to obtain an unabridged perspective and be able to face antimicrobial resistance.

Keywords: Antimicrobial Resistance (AMR)
Rational drug use, Veterinary drugs

Objective. To disclose methods and/or monitoring by regulatory authorities for control and transmit the rational use of veterinary Drugs Against the Antimicrobial Resistance.

Methodology. The research has been developed through online tools from official websites aiming to face antimicrobial resistance. Documents in all languages were taken into consideration.

Results. All cited information from scientific articles and communicates and/or strategies by international organizations have a common denominator, a fair and constant action to eradicate antimicrobial resistance, confirming with it that this is a worldwide problem for which we are obliged to join efforts, transmitting and making a good use of antimicrobial drugs.

Conclusion. Currently, the inadequate use of antimicrobials has been widely studied globally, it has tools, plans and useful alternatives to face the growth of AMR in the short or long term.

Introduction

The rational use of veterinary drugs, particularly antimicrobials, is essential to guarantee animal health and prevent resistance or AMR. Incorrect drug administration in animals does not only compromise treatment efficacy but also contributes to the development of resistant bacteria which could spread from animal to humans, threatening public health. The growing concern about the excessive or inappropriate use of antibiotics in livestock has brought the implementation of policies that promote a more efficient and sustainable approach (ANIMUSE (s.f))

In animal healthcare, prophylactic and metaphylactic use of antimicrobials in production animals has been a common practice for decades. However, these practices have been pinpointed as key factors in the selection of resistant bacteria which highlights the need to adopt stricter strategies to control and reduce the unnecessary use of antibiotics (European Medicines Agency, 2021).

In Europe, initiatives such as the program REDUCE from SPAIN, have been implemented to decrease the consumption of antibiotics in species such as porcine and bovine, achieving important milestones in reducing the use of these drugs in animal healthcare (PRAN (s.f)).

The "One Health" perspective, which recognizes the interrelation between animal, human and environmental health, is key to approach the AMR challenge. In the veterinarian context, this implies the development of therapeutic guidelines, conveying disease prevention through vaccines and improvements in husbandry as well as communicating non-antimicrobial therapeutic alternatives (Aarestrup FM, 2005).

Method

To create this literary review research included articles, international organisms communicates such as the World Animal Health Organization (WAHO), Food and Agriculture Organization (FAO), World Health Organization (WHO), and scientific literature through: Cochrane, Google Scholar, based on different plans to confront Antimicrobial Resistance. The aforementioned would answer the following question: Which control or measures exist to manage rational veterinarian drug use against Antimicrobial Resistance?

One factor to consider when selecting cited articles and studies was the publishing cite to guarantee the content has been duly peer reviewed and approved, containing the material that caters the topic's needs. Articles in all languages were considered using translation software when needed to obtain the most accurate results.

Discussion

Article research made evident that there is ample information about the efforts conducted through time by different entities or international organizations to control the antimicrobial resistance within veterinarian medicine. Nevertheless, through history the amount of microorganisms is on the rise, establishing the need to educate the involved parties, such as: breeders, sellers, owners and general public to raise awareness about health and infection prevention being achieved by far more than administering drugs as prophylactics or growth promoters (in case of avian industry), thus, making it vital to advocate for accurate diagnosis through laboratory tests to help back up the need to use antibiotics as specific treatments.

It is a global interest to look for measures that work to diminish the antimicrobial resistance in accordance with entities such as the World Animal Health Organization (OMSA) to generate information that is interesting and control measures including different plans and surveillance systems, as well as awareness campaigns about rational antimicrobial use.

On the other hand, as part of the commitment against AMR, El Salvador as an active member of the OMSA has followed up the use of the platform ANIMUSE, where continuous reports about the consumption of antimicrobials are posted and their objective is to regulate and monitor their rational use as much as possible.

General Information

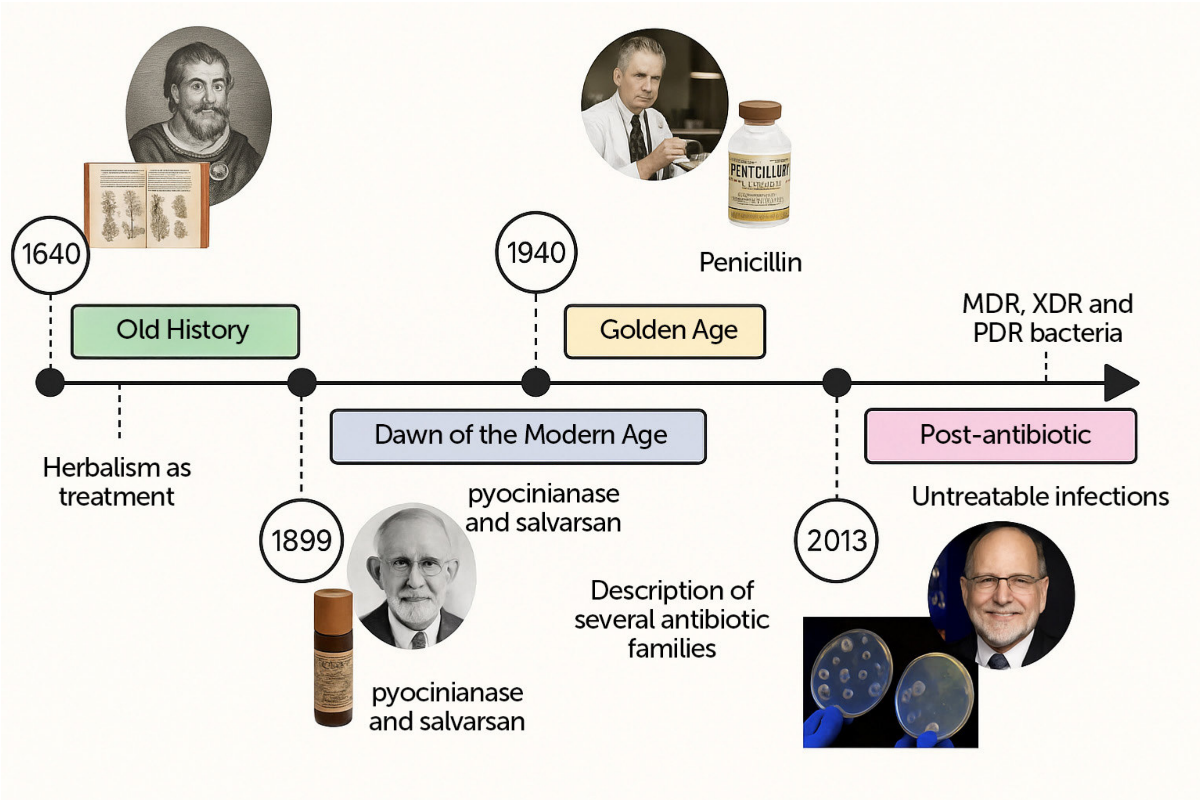
What is antimicrobial resistance? How long has it been around?

Antimicrobial resistance (AMR) refers to the microorganisms ability to endure antimicrobial treatments (Barton MD, 2014). It is one of the main healthcare challenges of these times being a cause of death around the world. It is presented as a constant threat for animal and human health, as well as for homes sustenance and food security worldwide (Camacho Silvas LA, 2023).

The so-called "superbacteria" are a true challenge for healthcare professionals, veterinarians and other animal healthcare professionals, due to the decreasing rates of effective therapeutic options to prevent, control, and treat infectious diseases. Once again, animals and people are becoming defenseless against infections.

Since the discovery of penicillin in 1928, many investigations have been developed, mainly to identify the mechanisms and causes that make this resistance possible just as the development of new tactics to minimize the damage whether it is through new pharmaceutical products or by streamlining programs for these pharmaceuticals (Cameron A, et al. 2016). Although this discovery was made in 1928 the different discoveries of antibiotics and their bacterial resistance first started way before as shown in Figure 1.

Figure 1. Antibiotics discovery timeline and the beginning of bacterial resistance (Cameron A, et al. 2016)



How do bacteria become drug resistant?

It is about the race between the people who look for the cure of diseases and the germs as bacteria that evolve to survive. Antibiotics have an objective to kill or limit the growth of bacteria which makes animals and people sick. Mastitis in milk cows, respiratory infections and urinary tract infections in dogs and the Staphylococcus infections in fish are infections that must be avoided to reduce the suffering and death in animals.

The evolutionary advantage acquired by new resistant variants could prosper and spread through natural selection. Each time antibiotics are used bacteria have the opportunity to become resistant. Does this mean we have to stop using antibiotics? No but it does mean we have to use it responsibly and only when it is needed. (Camacho Silvas LA, 2023).

It is important to point out that with time bacteria adapt very well to their environments due to genetic mutations and and the transfer of an antimicrobial resistant trait, sometimes they can acquire genes that allow them to survive to drugs used to fight them due to genetic mutations and antimicrobial resistant traits (Camacho Silvas LA, 2023).

In the following table are summarized some resistance mechanisms adopted by bacteria due to the misuse of antibiotics.

Table 1. Germ spread and resistance mechanisms

Resistance Mechanisms	Description
Restricting access to antibiotic	Germs restrict the access, changing the entryways or limiting the number of entries. For example: gram negative bacteria have an external membrane that protects them from the environment. These bacteria can use this membrane to selectively stop the entrance of antibiotics
Disposing of the antibiotic or antimycotic	Those disposal of antibiotics through bombs and their cellular walls to eliminate antibiotics that go into the cell. For example: some *Pseudomone aeruginosa* bacteria can produce bombs to eliminate several important antibiotics, including fluoroquinolones, beta-lactamase, Chloramphenicol, and trimethoprim. Example: some *Candida* species produce bombs that eliminate azoles as fluconazole
Change or destroy the antibiotic	Change modifier destroyed antibiotics with enzymes, proteins that decompose the drug. For example: the bacteria *Klebsiella pneumoniae* produces enzymes called carbapenemases, the decomposed carbapenemic drugs and most of all other beta-lactamase drugs.
The change antibiotic or antimycotic aim	Many antibiotics are designed to attack and destroy specific parts of a bacteria. Germs modify their antibiotics aim in a way that the drug cannot fit and do its job. For example: *Escherichia coli* bacteria with the gene MCR -1 can add a compound to the exterior of the cellular wall so the colistin drug cannot adhere to it. For example: *Aspergillus fumigatus* changes the gene CYP 1A so triazoles cannot adhere to the protein.
Avoid antibiotic effects	For example: *Escherichia coli* bacteria with the gene MCR -1 can add a compound to the exterior of the cellular wall so the colistin drug cannot adhere to it.

Note: adopted from Centers for Disease Control and Prevention CDC. (2024, June 3rd). About antimicrobial resistance. https://www.cdc.gov/antimicrobial-resistance/about/index.html

How does antimicrobial resistance affect animals? It is necessary to understand that antimicrobial resistance can originate in minor species like pets, major species and human beings. Next some articles are cited to help understand better how antimicrobial resistance in animals is generated.

Minor species

In industrialized countries, the number of pets has significantly increased in the last few decades and it is expected for it to keep growing. The role of company animals is changing, and consequence, a greater attention to animal health and hygiene will drive to general improvements and animal well-being (Clifford K, et al. 2018). On the other hand, aggravated contact between animals and humans brings a greater risk of infection and transmission of antimicrobial resistant traits. Hence, the possibility of reversing zoonosis with the creation of animal reservoirs that support the infection cycle and antimicrobial resistance spread, is now a growing threat. (Cromwell GL, 2002), (Deusch S, et al. (2014). Animal antibiotic resistance poses a direct or indirect threat to human health. Staphylococcus aureus represents methicillin resistance, as well as staphylococcus, enterococcus are resistant to vancomycin, enterobacteria producers of carbapenems and gram-negative extended-spectrum beta-lactamases (Doster E, et al. 2018). A 24 month detection study was made to determine the prevalence among is *Staphylococcus spp* resistant to methicillin in pets. The study was carried out on 20,366 dogs and 8,026 cats that showed alarming rates of methicillin resistant traits. 40% of resistant staphylococcus were identified as *Staphylococcus schleiferi,* 35% *S. aureus* and 17% *Staphylococcus intermedius. S. intermedius* isolation occurs most frequently in cases of dermatitis and auditory canal infections, mainly in dogs. An equally resistant *S. intermedius* strain has been isolated mostly in dogs; whereas the spread of infections by methicillin resistant *Staphylococcus aureus (MRSA)* is linked to deep-seated infections that occur at similar rates in both cats and dogs. These remarks are mostly due to antimicrobial therapy in pets, which suggests excessive use of antibiotics is one of the main reasons for the origin and spread of antibiotic resistance. Currently, many epidemiological studies are being carried out to monitor the incidence and spread of antibiotic resistance. Nevertheless, these epidemiological parameters cannot be clearly defined because they are influenced by a series of variables, including the population's characteristics, the geographical position, and the research methods used for the study (Appl Environ Microbiol, 2008). Independently of epidemiological data, there are more tests suggesting it is necessary to study the ways in which microorganisms express and/or transmit antibiotic resistance. From this perspective, the excessive use of antibiotics on their own is not enough to provoke a massive spread of antimicrobial resistant microorganisms between animals and humans (Ejecutivo, D, 2023).

Major Species

Traditionally, antibiotics in livestock are used to treat communicable diseases, as well as to develop preventive care and as growth stimulants (Giguère S, et al. 2013). Although a clear mechanism for this phenomena is not completely understood yet, it has been observed that the prolonged use of antibiotics in subtherapeutic doses affects multiple organs and reproductive physiological processes, which takes us to: a decreased biodiversity within gastrointestinal microbiota and decreased nutrient absorption capacity, reduction in harmful bacteria, reduced stimulation of the immune system, increased vitamin biosynthesis at an intestinal level and altered metabolism (Klous, G, et al. 2016).

Altogether, these results bring about improvement in the net energy balance and, in consequence, in animal productivity from a technical point of view. Nonetheless, the use of antibiotics as growth stimulants cannot destroy harmful bacteria entirely (Gyles CL, et al. 2008). Also, antibiotics sublethal doses act as a selective pressure, stimulating bacterial evolutionary mechanisms to adapt to stressful environmental conditions thus allowing more resistant specimens to exist and spread with antibiotic resistant traits. To avoid this problem, since 2016, the European Union has forbidden in its entirety the use of antibiotics as growth promoters.

The use of antibiotics as disease prevention also has a similar effect (Loeffler, A, 2010). From this perspective, antibacterial compounds are used often in tap water or in kibble which exposes animals to low doses through long periods of time. However, the protective effect reverts when these are withdrawn and animals are still susceptible to infection (Gyles CL, et al. 2008).

The prophylactic use of antibiotics in livestock farms include oral administration, mainly to prevent respiratory diseases and/or hepatic abscesses (Marshall BM, et al. 2011). In addition, wide spectrum antibiotics are injected into the udder during the no-breastfeeding period to reduce/prevent the incidence of mastitis in lactating animals (Gyles CL, et al. 2008). In pig farming, antibiotics are used to prevent diseases. Pigs are usually kept in homogeneous groups in age, size and weight which makes massive antibiotic treatment easier, especially during maximum susceptibility periods (Messenger, A. M, et al. 2014), (Morris, D. et al. 2006). These stages are from birth to the first lactation, during this period, animals face stressful procedures and are potentially infectious, such as the cutting of umbilical cord, tail or teeth. Likewise, it is considered susceptible to getting sick during vaccination and sterilization period; therefore, prescribing wide spectrum antibiotics helps reduce the general risk of infection (Gyles CL, et al. 2008), (WHO Critically important antimicrobials for human medicine 6th revision. 2018), (World Health Organization. 2016). Additional antibiotic uses in veterinarian medicine are linked to the treatment of communicable diseases. Ideally, therapeutic interventions are developed after precise identification of pathogens and antibiotic susceptibility tests (e.g. antibiogram), (World Organisation for Animal Health (IEO), 2016)

However, the common practice of administering antibiotics to the complete herd to limit pathogen spread brings about the excessive use of antibiotics because animals that have not been affected are also treated (Gyles CL, et al. 2008). Most recurrent infections in livestock farms are caused by shipping fever, bovine pneumonia and diarrhea, which require general use of common antibiotics such as: penicillin, quinolones, gentamicin, and tylosin (Palma E, et al. 2020). Moreover, wide spectrum antibiotics are often used to treat hepatic infections, whereas reduced spectrum antibiotics, such as betalactamases, are the first option to treat streptococcal mastitis (Parisi A, et al. 2019). At a worldwide level, using antibiotics as treatment in pig production is quite low when compared to growth promotion antibiotics or prevention (Pomba, C, et al. 2017). The most common infections among pig farms are gastrointestinal in nature and are linked to penicillin, tetracycline, aminoglucosides, and quinolones. Also, great amounts of tiamulin, lincomycin, and enrofloxacin to treat zoonotic pneumonia which is different from pig dysentery and ileitis (Gyles CL, et al. 2008), (Critically important antimicrobials for human medicine, 6th revision 2018, World Health Organization. 2016).

In poultry, antibiotics with medicinal uses are usually within drinking water. Some commonly used are penicillin, aminoglycosides, tetracyclines, macrolides and sulfonamide/trimetoprim combination (Rao S, et al. 2010), (Rendle, D. I. et al. 2018). Besides, similar antibiotics are used in sheep and goat farms (WOAH Antimicrobial Resistance, 2022)

According to literature, raw milk has been established as a relevant source of human infection by *Arcobacter spp.* The consumption of thermally treated milk and the use of pasteurized milk in dairy products should be effective measures to prevent risks in human health. However, the risks of generalized consumption of raw dairy products in human health must be considered, especially since it has been discovered that, in some of them, for example, in ricotta and mozzarella cheese, have many Arcobacter spp capable of enduring the temperatures used for its manufacturing (WOAH Antimicrobial Resistance, 2022)

Understanding the fine dividing line between the different veterinary and human pathogens; it is important to recognize the bacterial specimen responsible for relevant infections, which are summarized in Table 2.

Table 2. Major microorganisms responsible for relevant infective disease and AMR onset and diffusion.

Resistant Bacteria	Isolation Source	Antimicrobial Compound(s)	Major Resistance Mechanism
Campylobacter spp.	Cattle, Chickens, Turkey, Pig, Sheep, Dog, Cat, Horse	Quinolones, Macrolides, Lincosamides, Chloramphenicol, Aminoglycosides, Tetracycline, β-lactams, Cotrimoxazole, Tylosin	Point mutation on GyrA gene, CmeABC multidrug efflux pump, Methylation of ribosomal target, Point mutation in the ribosomal target
Salmonella spp.	Human, Chicken, Turkey, Pig, Cat, Dog, Horse	Tetracyclines, Sulfonamides, Streptomycin, Kanamycin, Chloramphenicol, β-lactams, Amoxicillin/clavulanic acid, Nalidixic acid, Ceftriaxone	Multiple point mutations on GyrA and GyrB, parC, and parE genes; AcrAB-TolC multidrug efflux pumps; Changing outer membrane proteins; qnr genes-containing plasmid; Salmonella Pathogenicity Island-1 and -2
Staphylococcus spp.	Human, Farm animals, Dog, Cat, Horse	Penicillin, Methicillin, Vancomycin	Staphylococcal Cassette Chromosome-mec genes (SCC-mec)
Enterococcus spp.	Human, Farm animals	Vancomycin, Aminoglycosides, Penicillin, Chloramphenicol, Erythromycin, Tetracyclines	lsa gene
Other Gram-negative	Human, Farm animals, Pet	β-lactams	Extended-spectrum β-lactamases

Note: Taken from Palma E, Tilocca B, Roncada P. Antimicrobial Resistance in Veterinary Medicine: An Overview. Int J Mol Sci. March 11th 2020 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7139321/#B55-ijms-21-01914

Integrated surveillance of antimicrobial resistance (AGISAR) (Tilocca B, et al. 2020)

Due to the evident growing issues, an effort was made to establish a critically important antimicrobial for human Medicine.

The first CIA WHO list, was prepared in 2005 and other revisions were made posthumously in 2007, 2009, 2011, 2013, 2016 and 2018 (current version) with some modifications.

During the first meeting, held in Canberra, Australia, in 2005, the participants reviewed a list of all antibiotics used in medicine and obeys to two criteria defined in the same meeting, then proceeded to their classification in three groups: critical importance, important, and very important.

In a second meeting, held in Copenhague, Denmark, in 2007, the first two criteria from the first meeting were reviewed and examined again the categorization of all the types of antibiotics for human use depending on the development and research of new drugs, with information received after 2005. It was also asked from the participants to prioritize the "Important antimicrobial" medications, to focus the necessary resources on the antimicrobial resistance management for those drugs considered more essential and it was denominated "Highest priority critically important antimicrobials" to the ones that meet all prioritization criteria.

Afterwards, in 2009, a worldwide call to several experts on relevant fields were called, among them included public health and veterinarian medicine, to establish the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR), to review and update the CIA list that the WHO has made available.

During the third AGISAR meeting held in Oslo, Norway, in 2011, the WHO list by the CIA with additional information was updated. The aforementioned tables also include veterinarian medications that belong to the same categories as the ones used in humans to help risk managers to easily identify classes and similar drugs to the ones used in human healthcare and that have a greater impact in significant human medicine antimicrobial resistance.

In the fifth AGISAR meeting, held in Bogotá, Colombia in 2013, the WHO list by the CIA was once again updated, and also during the seventh AGISAR meeting, held in Raleigh, USA in 2016. During the latter, minor changes were made to the Priority Criteria, aiming to better describe the use of antibiotics in hospitalized patients with severe diseases when there are few to non-existent alternative treatments. As a result, the polymixins, due to the increase in colistin use have been placed in the category of "Highest priority critically important antimicrobials" since it is used to treat severe infections in humans within many regions of the world, also the the spread of resistant bacteria into the food chain, as well as the discovery of genes that provide drug resistance.

Since, up until now, pleuromutilin has only been used topically in humans and resistance to methicillin by Staphylococcus Aureus has not been transmitted (SAMR), from no-human sources, these antimicrobial drugs has been reclassified as "important".

As a result of this many lists were obtained and they are useful to apply significant changes and special considerations to use drugs from veterinarian and human use.

What type of measures or surveillance techniques for a correct usage of antimicrobials exist for a good use of them?

SURVEILLANCE

1. National
Plan to control Antibacterial Resistance in El Salvador (Salvador, S., et al (s/f)

The National Commission against Antimicrobial Resistance founded on January 23rd, 2015, is made up by the following institutions: Ministry of Health, Sanitary Regulation Superintendency, Public Health Council, Salvadoran Social Security Institute, National Healthcare Forum, University of El Salvador, Infectology Salvadoran Association, Medical Collegiate of El Salvador, Salvadoran Microbiologists Association, PAHO, Military Health, Agriculture and Livestock Ministry and the Salvadoran Institute for Magistral Healthcare.
The National Commission against Antimicrobial Resistance aims to guarantee adequate use and access to antimicrobials, prevention, decrease and timely management of multidrug-resistant microorganisms through individuals' coordinated actions. With these awareness is raised and it generates understanding of antimicrobial resistance through communication, education and effective instruction, through the strengthening of knowledge and evidence that is based on surveillance and research, reducing the incidence of infection. All these allow the promotion of streamlining antimicrobial use in human and animal healthcare, thus ensuring self-sustainability in activities destined to the adequate use, access and availability of antimicrobials to prevent, identify, provide timely and adequate treatment to multidrug-resistant microorganisms and other preventive measures such as immunization according to the identified needs in the country.

2. International
In a global context, the countries have committed, in the World Health Assembly 2015, to apply the established framework within the Global Action Plan on Antimicrobial Resistance from 2015, and to elaborate and implement multisectorial national action plans. The Plan was afterwards approved by the FAO and WOAH representatives with the purpose to ensure global progress, the states must consider financial and application of national action plans in several sectors to guarantee sustainable progress. The WHO Global Strategy for Containment of Antimicrobial Resistance, made in 2001, offers an intervention framework to slow the progress of said resistance and reduce its spreading (Tröscher-Mußotter, et al. 2019).

- Global Action Plan on Antimicrobial Resistance

The One Health concept brings together several interested parties in human healthcare, aquatic and terrestrial animals, plants, feed or fodder production, human food production for the population and the environment to establish communication links, and collaborate with the creation and implementation of programs, policies, legislation and research to improve public healthcare (Tilocca B, et al. 2020).

The World Health Organization is working hand in hand with FAO and WOAH to apply One Health thus promoting ideal practices contributing to decreasing antimicrobial resistance and reducing its development.

This plan has 5 objectives: raising awareness and understanding of antimicrobial resistance through communication, education, and effective literacy as well as strengthening knowledge and scientific basis through surveillance and research to reduce the incidence of infections through effective sanitation measures, hygiene, prevention and using antibiotics adequately (Tilocca B, et al. 2016).

- World Antimicrobial Resistance Awareness Week (Tilocca B, et al. 2020)

This week used to be called «World Antibiotic Awareness Week». However, since 2020, it has been called "World Antimicrobial Resistance Awareness Week". In this activity a global campaign is carried out to sensibilize on antimicrobial resistance at a worldwide level and share the best practices among the general public, healthcare workers and the legislators to reduce the spreading of pharmaceutical resistant infections.

The Tripartite Executive Committee decided to establish all dates for the next world awareness weeks from the 18th to the 24th of November and the slogan for the World Antimicrobial Resistance Awareness Week 2024 is "Educate. Advocate. Act now". The topic this year summons the world community to promote the relevant sectors on AMR, advocate for effective commitment and adopt measures to face this issue.mana Mundial de Concienciación sobre la RAM (2024))

-Global Antimicrobial Resistance and Use Surveillance System (GLASS) (Tilocca B, et al. 2020)

The World Health Organization (WHO) implemented the Global Antimicrobial Resistance and Use Surveillance System (GLASS) in 2015 to keep knowledge and lead strategies at all levels, offering a standardized perspective for compilation, analysis, interpretation and data exchange through countries, territories and zones, thus allowing surveillance over national systems whether they are new or pre-existing, to guarantee representation and excellence from the obtained data.

The GLASS System has been conceived to progressively incorporate data from the AMR surveillance in humans, the use of antimicrobials, and the resistance in the food chain and the environment.

ANIMUSE (ANIMUSE. (s/f)

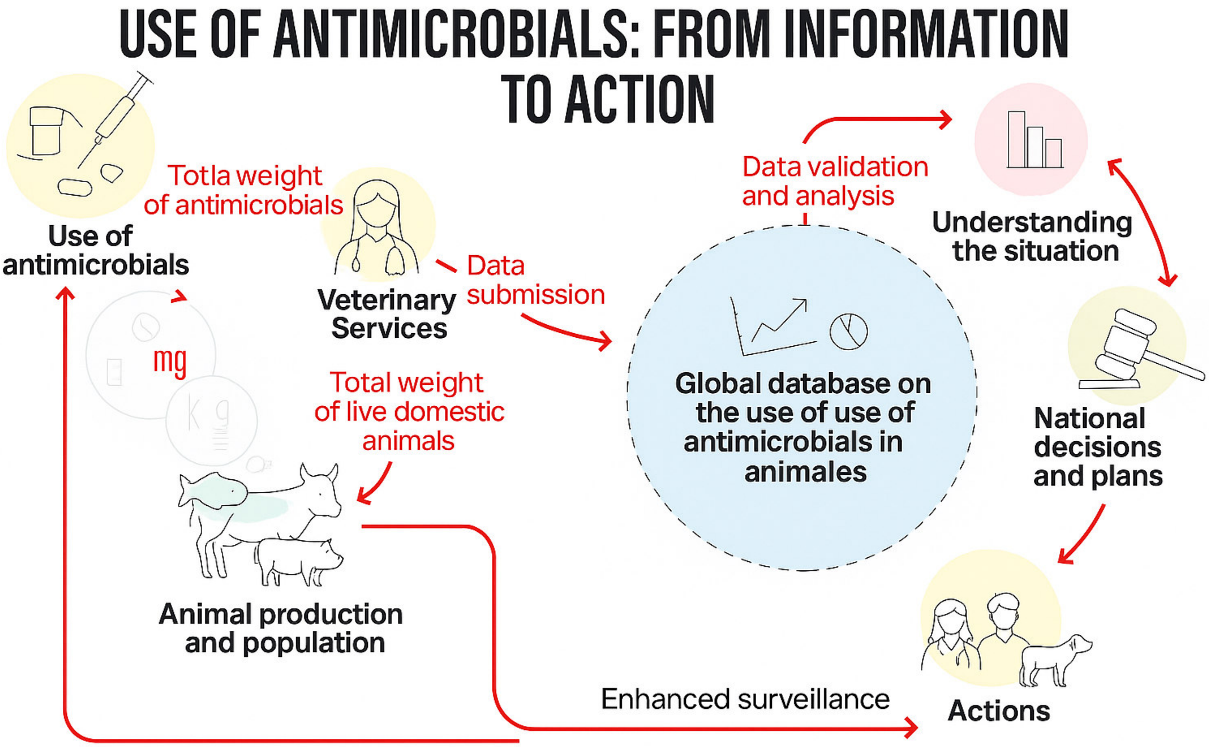
The World Organization for Animal Health (WOAH), has been gathering data about figures and motives to use antimicrobials in animals since 2015. This information constitutes an essential means to diminish the overuse and misuse of drugs such as preventing the spreading of Antimicrobial Resistance (AMR).

ANIMUSE is a platform that contains the global database on antimicrobial use in animals, eases the access to this relevant information in constant evolution.

Countries can communicate, access, analyse, and interpret data on antimicrobials used in animals through this automatized interactive database online. It offers basic tools to generate reports, detect errors and visualize data. As a last resort, its objective is to improve the use of antimicrobials in veterinary medicine and in aquatic animals' health.

The presentation of reports is open to all countries, whether they are WOAH members or not. National veterinary services could provide general information and, in case of counting on quantitative information, they have many options depending on the level of detail in their data.

Figure 2. Data collection process infographic (ANIMUSE. (s/f))



Preventive Measures (Camacho Silvas LA, et al. 2023)
Solution: prevention and responsible antimicrobial use

Even when the way to stopping antimicrobial resistance appears challenging there is already a set of preventive measures to achieve it. Measures that cover animal health, livestock, aquatic animal producers, pet owners and relevant professionals to ensure these drugs are used responsibly and continue being effective in the future.

Given that animals are more prone to illnesses according to the environment quality where they live and stress factors, it is worth using good agricultural practices focused in disease prevention and responsible antibiotic use thus collectively limiting the spread of antimicrobial resistance protecting their efficacy. A growing number of livestock and animal health professionals are changing their practices to successfully face the threat posed by antimicrobial resistance. These efforts are reassuring and protect everyone.

Firstly, the use and prudent management of antibiotics are undoubtedly useful to delay antimicrobial resistance, however, even if the European Union (EU), has applied restrictive measures in the veterinary field, such as forbidding growth promotion antibiotics, and tracing antibiotics, no significant improvement has been reported suggesting the need of a joint intervention among the different sectors and a global effort in the acquisition and/or compliance of regulatory measures.

It is also required to adopt adequate prophylactic interventions, such as immunization, although it is not capable of protecting against specific pathogens as the prophylactic use of antibiotics does, it does reach a reduced group of infectious agents and reduces the transmission of AMR. Now, vaccination programs cannot be considered a total solution, and it is necessary to have complementary alternatives for a non-therapeutic handling of husbandry. An option to prevent infectious diseases is represented by the opting for adequate probiotics and/or prebiotics that act directly over the intestinal microbiota which can improve all immune system and its protective functions, maintaining a better feed conversion and a greater chance against colonization by pathogens (Van Boeckel, et al. 2019), (Varela NP, et al. 2013).

In this way, many research lines are being developed to discern the dynamic composition and the intestinal microbiota mechanisms and guide the selection of suitable probiotics and prebiotics.

Another option to prevent communicable diseases is based on the use of bioactive peptides with bacteriostatic or bactericide effects. Nisin A, a naturally produced bacteriocin by lactic bacteria, has shown promising results, being harmless to mammals and efficient in controlling pathogen specimens. The collected evidence showed the bacteriocins efficacy in the food industry as well (Woolums AR. 2018). Currently, studies are being conducted to evaluate the in-vivo bacteriocins stability, as well as the most suitable administration strategy.

Regulatory Agencies

The role of regulatory agencies in evaluating the risk-benefit ratio in new drugs or combinations is of utmost importance since said products can represent harm to human, animal and environmental health if they are not compatible with the posology, instructions, and destined species for which their efficacy has been proven. It is the regulators duty to ensure the safety, efficacy and quality of products through the implementation of standards and norms to be able to harmonize them along the region, requirements, and back up documentation to present to justify different combinations or innovative drugs, as well as the strengthening of different technical capabilities among the general population about the overuse or misuse of drugs, to keep a constant surveillance, to identify different patterns and trends in the use or registration of antimicrobials, fostering research, among others.

Conclusions

Currently, the misuse of antimicrobials has been widely studied around the world. It has tools, plans and useful alternatives to stop, short or long term, the growth of AMR. However, it is necessary to articulate a better performance among all parties involved (veterinarians, pharmaceutical industry, regulators, distributors, producers and pet owners), to have further the communication of information that refers to Antimicrobial Resistance and the rational use of medication among the general public, intending to raise awareness and avoid an increasing rate of cases due to misinformation or misuse of drugs.

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