REDVET - Revista electrónica de Veterinaria - ISSN 1695-7504
Vol 24, No. 3 (2023)
http://www.veterinaria.org
Article Received: 10 September 2023; Revised: 20 October 2023; Accepted: 09 November 2023

Antibiotic Resistance Growth: Investigating the Consequences of Defective Veterinary Pharmaceuticals

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Abstract

Antibiotics are commonly employed in farm animals to promote growth and prevent illness, which leads to the emergence of resistant bacterial strains. The study examines substandard veterinary medications, highlighting the potential for incorrect dosage and bacterial eradication due to poor formulations and insufficient quality control. Antibiotics are used in farm animals for infectious illness prevention, with tetracycline as the most commonly used class. With the goal of minimizing the emergence of resistance in veterinary care by minimizing the usage of antibiotics in 2019, mandatory guidelines for the careful use of antibiotics in animals were released. These recommendations outline the minimal standards that veterinarians must adhere while giving antibiotics to animals. The administration of antibiotics in accordance with precise criteria is one of their main components. The findings derived from a comprehensive monitoring study conducted by Veterinary Pharmaceuticals spanning the period from November 2019 to April 2021, which tracked the utilization of antibiotics in veterinary pharmaceuticals, as medicated feeding ingredients, reveal a notable shift in veterinarians' prescription practices subsequent to the adoption of the guidelines. According to the decreasing usage of antibiotics, which dropped from 4366 kg prior to the recommendations to 1253 kg in the first quarter of 2012, the number of days each animal obtained therapy reduced from 31.7 to 13.7. The research found that the percentage of antibiotic prescriptions containing chlortetracycline decreased from 78% to 15.7%, indicating the adoption of veterinarians' recommendations as a tool to reduce antibiotic use and reduce resistance.

Keywords: Antibiotics, Farm Animals, Veterinary Pharmaceuticals, Consequences

INTRODUCTION

The consequences of defective veterinary medications should be thoroughly investigated as one potential contributing element to the growing worldwide problem of antibiotic resistance. This is a matter of great public health concern. Since the cattle business depends on antibiotics to prevent sickness and promote development, the appearance of inferior or inefficient veterinary medications raises serious concerns about how these medications contribute to resistance towards antibiotics (1). Antibiotic characteristics have been present since ancient times, as evidenced by the detection of Antibiotic resistance traits in mummies, secluded caverns and permafrost. Currently, innate and acquired antibacterial resistance (ABR) are used differently. The first is the outcome of microbial long and sluggish evolutionary processes to adjust to the shifting circumstances of their environment. Resistant spread is caused by plasmid-induced resistance (2). Figure (1) shows the evolution of bacteria's resistance to antibacterial, evaluation of genome genetic stability and the frequent discovery of refusal viruses in naturally occurring bacteria isolates, challenge the widespread belief that resistance-encoding elements quickly and easily disappear when antibiotic treatments do not exert any selective stress (3).

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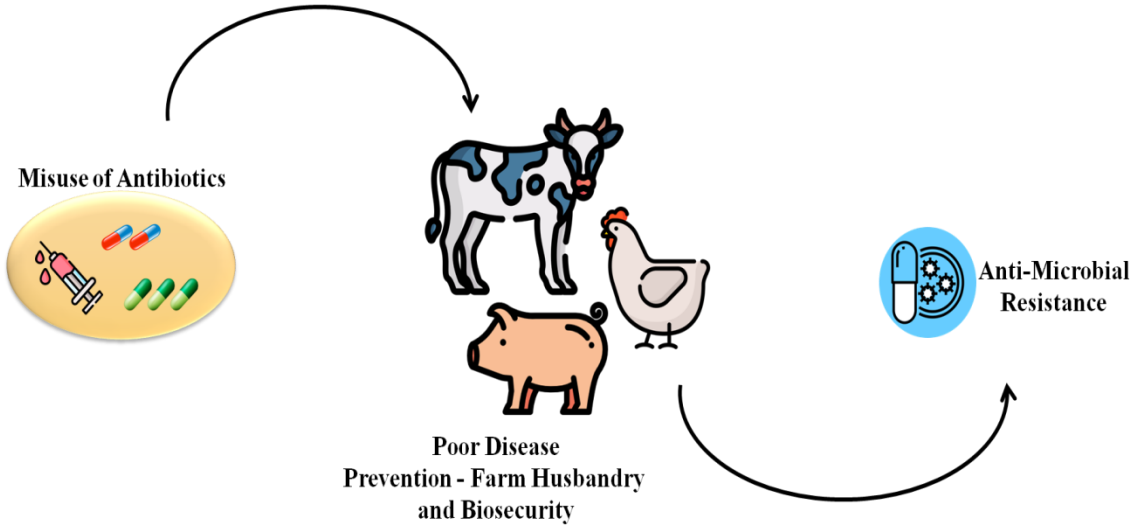

Figure (1). The evolution of bacteria's resistance to antibiotics

(Source: Author)

Microbial tolerance is defined based on certain laboratory cut-off values; the pathogen is classified as susceptible, intermediate, or resistant; this categorization is based on whether the pathogen has a mutant or acquired resistance mechanism. Antimicrobial function at a level linked to a high chance of therapeutic failure is referred as clinical tolerance (4). It means, in particular, that it is more effective to use a medication against a pathogen that has been tested and shown to be sensitive to treatment than it is to use a medication against a bacterium that has been tested and shown to be resilient uncontrolled access and use of over-the-counter medications, among other issues, can lead to the incorrect prescribing of antibiotics (5). A number of other variables contribute to the need for prescribed antibiotics. Due to the multiple resistance patterns germs that are Gram-positive and that are Gram-negative have created, treating infections with traditional antibiotics can be difficult or even impossible. When patients have pneumonia, numerous hospitals fail to identify the causing bacteria early enough to determine their sensitivity to antibiotics (6). Bacteria as treatments altered the development and dissemination of resistance by imposing strong selection pressures, particularly on human and domestic animal microbiota members as well as in antibiotic-polluted habitats (7). Such Antibiotic resistance genes (ARGs) have been mobilized and horizontally transmitted among several bacterial species due to selection pressure, with a focus on causing illness (8). These medications and injections can be added to food and drink or given as an injectable, pill, shower, or washing. There is recorded proof of past farming conventions and customs, including the fact that nomads provide animals with medicine. It is anticipated that by 2030, the utilization of therapeutic veterinary antibiotics (VAs) will surpass 100,000 tons. Manure production as a whole has increased along with the world's animal population growth. In the region, the member nations were anticipated to produce 1.4 billion tons of manure annually (9). Likewise, dung production amounts to billions of tons every year. Consequences of substandard veterinary medications on the advancement of drug resistance aims to offer important insights into the possible contributions of the agriculture sector to the worldwide antibiotic resistance dilemma by closely examining the relationship between inferior medications used in animal husbandry and resistance to antibiotics bacteria's rise to prominence (10). Examining the effects of faulty veterinary pharmaceuticals aims to determine the degree of harm that the use of inferior or faulty drugs in the veterinary business causes to public safety as well as animal health.

The study (11) provided the chemical make-up, useful uses as well as impacts on reproduction characteristics. Scientists, researchers, dietitians, biologists, embryologists, pharmacists, veterinarians, pharmaceuticals and animal breeders benefit from knowing this knowledge on the quality of semen and the outcomes of vitro fertilization. The author (12) presented an overview of the most important veterinary medication delivery

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methods based on polymers drug delivery methods based on hydrogels, films, microparticles, micelles, nanogels, nanoparticles, tablets and implants. They are highlighted among the conventional and novel polymer-based drug delivery methods offered. The author (13) provided a concise summary of the short-term and long-term effects of the five most prevalent Nonsteroidal anti-inflammatory drugs (NSAIDs): acetylsalicylic acid (ASA), paracetamol (PCM), diclofenac (DCF), ibuprofen (IBU) and naproxen (NPX) found in surface waters globally.

The study (14) investigated the impact on animal well-being in herds where antibiotic consumption has been reduced. They carried out semi-structured interviews with ten pig farmers and six pig veterinarians from Denmark. To protect animal welfare while keeping pharmaceutical consumption low was the overarching goal of the study. The author (15) suggested synthesizing the structure with the designed defects by including ethylene glycol in the solid-state synthesis procedure. The photocatalyst was studied using several methods for characterization. Led light illumination enhanced the photocatalytic efficacy of the macroporous structure in degrading tetracycline antibiotics.

Data transmission and reporting

Data on the quality of veterinary medicine is gathered at every stage of the supply chain due to portable, reasonably priced drug testing devices that enable quick evaluation of medication quality. A unified, easily available and open government system for veterinary care quality reporting has to be established to compile this data in a readable manner. Policymakers and other government representatives would have the data they need to create legislation and make decisions that have a significant impact (16). All farmers who purchase veterinary medicine must be informed of the information gathered on medicine quality. Safe supply chains and reasonable costs are essential for farmers to have access to high-quality veterinary care, which is necessary for them to make sensible purchasing choices (17).

Antibiotic use in veterinary medicine

There's a lack of information on the dosages of antibiotics used in animal medicine member countries, with the exception that a total of 3,585 tonnes of active substances were utilized as medicines on cattle. Tetracyclines made up part of 66%, penicillins made up 7%, macrolides made up 14% and the remaining antibacterial families combined made up 14%. In contrast to human medicine, newer, more powerful antibiotics like fluoroquinolones and third-generation cephalosporins are employed extremely seldom 1%. At the same time, 7548 tonnes of antibiotics were thought to be used in human medicine (18). In 2007, several antimicrobial feed additives were outlawed; Table (1) debits the antibacterial medicine dose and volume, leading to a 53% decrease, to 658 metric tons, in the 405 metric tons of antibiotics used for veterinary treatment, while their non-therapeutic use as growth boosters in cattle increased. According to estimates, there are about 6.8 times as many food-producing animal species as there are humans.

Table (1). Antibacterial medicine dose and volume (Source: Author)

Information	Antibiotics 2018, 2020 population (2019)	Livestock, sheep, chickens, men (70 kg), medication and treatment days
Persons	8258, 7768	Body weight (23 490) Number (374 x 10^8)
Animals	4905, 4349	Body weight (kg x 10^8) Number (x 10^8)

This is seen in the dosages of 352 and 58 mg antibiotic/kg body mass/year for cattle, sheep, goats, pigs and poultry, creatures showing that human medicine uses therapeutic antibiotics more frequently than it does for treating farm animals. Even while livestock receive less antibiotic treatment than humans do, the circumstances surrounding their use of these drugs encourage the emergence of tolerance (19). In calves, pigs and poultry, oral therapy is used for practical reasons and medicated drinking water along with food items are used to provide

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around 85% of the antibiotics. Long-term treatment of whole animal herds is possible with this application method. While less than 25% of patients receive individual injectable medication, oral flock treatment is more than 85%.

Identification after the market

Authorities' stakeholders in low and middle-income nations should be made aware of the problems associated with subpar veterinary care by organizations that address antibiotic resistance. This will encourage these nations to make veterinary care a top priority and give them secure supply chains. Many global health programs are prioritizing innovative approaches to pharmaceutical supply chain management; this is an excellent chance to make sure that these advancements are used in veterinary medicine (20). By enabling regulatory authorities to test and respond quickly at the point of testing, portable technology that can evaluate the quality of medication might stop subpar veterinary medicine from reaching the market. Post-market testing needs to be used in conjunction with strict laws, penalties and repeat offenders' prosecution to have a lasting effect.

Verification of quality

When it reaches the customer, veterinary medication travels via several channels and it is dependent on numerous parties in the supply chain. There are several places where quality jeopardized and in many cases, distribution monitoring systems are insufficient. Governments might hold producers of veterinary medication to high standards for both local and import, yet they should be ready to impose penalties or refuse shipments in the event that a medicine lot fails quality tests (21). Agencies entrusted with testing at domestic production facilities and ports of entry would face fewer obstacles if new technologies to evaluate medication quality in the field at a reasonable cost were developed, making speedy on-site testing a more appealing alternative. Figure (2) show that the antibiotics and antimicrobials countries looking to establish quality assurance systems for veterinary treatment might get guidance from the Animal Health Organization of the World. Under the International Cooperation on Integration of Technical Requirements for Registration of Veterinary Medicinal Products initiative, a worldwide standard for veterinary medicine is produced. This project assists nations with drug registration procedures (22).

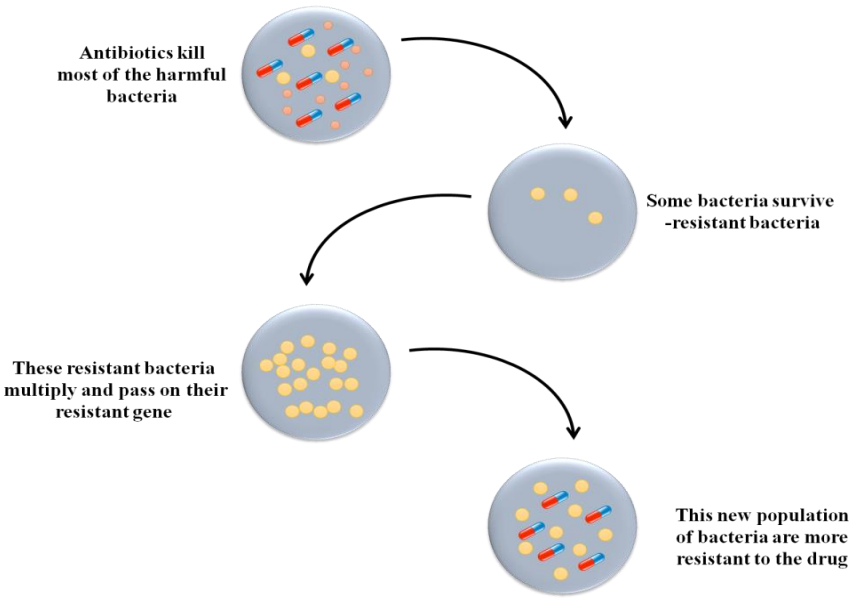

Figure (2). Antibiotics and antimicrobials

(Source: https://www.teagasc.ie/animals/amr/what-is-amr/)

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Each country is represented by a regional expert in animal medicine and Health with the international veterinary product network set up by animal products. It is important to adhere to the following rules when employing phenotypic techniques for "Determination of the sensitivity of microorganisms to antibacterial drugs". It is necessary to follow storage rules, use antibiotics with known levels of action and closely monitor the quality of nutritional media. The best method for studying antibiotic resistance in this situation is to use molecular genetics technique, especially in the following cases: investigations into acute and chronic infection outbreaks related to healthcare delivery; validation of results from phenotypic intraspecific typing (AR) techniques meant to identify hospital strains and monitoring the spread of global epidemic clones with the molecular genetics techniques are highly sensitive and quick in producing data and they are intended to uncover genes linked to resistance.

Even while animals receive less antibiotic treatment than humans do, farm animals' exposure to antibiotics encourages the emergence of resistance. For practical reasons, dentistry is given to calves, pigs and fowl. Drinking water and medicated feeding items are used to give over 77% of the antibiotics. Long-term treatment of whole animal herds is possible with this particular method (23). Injectable therapy for individuals is less than 30% and oral flock treatment surpasses 70%. When used on a large number of animals over an extended period, preferentially wide-range antibiotics strongly inhibit the emergence of bacterial resistance. Another problem with large-scale pharmaceutical feed water potential for unintentional low dosage because of decreased accessibility, such as inhomogeneous mixtures, drug chemical degradation, unfavorable medication conversations, decreased feed consumption by sick animals and interactions with feed components up to 30 days of therapy appear to indicate some careless usage of antibiotics. Table (2) represents animals given medication-infused food that contains antimicrobials. Over 60% of the treatments involved an antibiotic treatment for disease prevention, which is generally for non-specific reasons.

Table (2). Animals given medication-infused food that contains antimicrobials (Source: Author)

Antibacterial Organizations Total (Kg)	**Tetracyclines**	**Sufamide/ trimethoprim**	**Lincosamides and macrolides**	**Tiamulin**	**Fluoroquinolones**	**Colistin**
23064	67.3	33.3	4.2	3.2	0.07	3.8

Veterinarian's embracement of the antibiotic stewardship recommendations

Veterinary practices are obligated to increase their production of accurate clinical and microbiological diagnoses, possess in-depth knowledge of the characteristics of antibiotics, maintain a suitable stock of different antibiotics and be prepared for evidence. The best way to assess how the recommendations have affected veterinarians' attitudes toward prescribing antibiotics is to conduct a thorough monitoring program that tracks the emergence of resistance and the use of medicines meant for various animal species (24). A mechanism to track the use of antibiotics has not yet been developed. In the recommendations' introduction, one survey regarding the usage of food materials treated with antibiotics has been conducted. An evaluation was conducted on 1077 prescriptions for antibiotic-medicated feeding materials intended for pig fattening during the trial; the number of treated animals was relatively steady, averaging 251,000 pigs every quarter with typical seasonal fluctuations (25). These animals made up around 40% of the state's overall pig production medications each quarter steadily decreased, from around 360 to 260 in the most recent quarter. At the same time, the quarterly prescription volume of antibiotics fell by 74%, from 4366 to 1253 kg. The primary reason for this significant decline was a sharp decline in the usage of chlortetracycline, which was used in 78 % of cases at the start of the monitoring period but was used in 15.7 % of cases at the end. Only a portion of the decreased usage of chlortetracycline was offset by the prescription of alternative antibiotics, such as the more recent macrolide tilmicosin, which has a more limited antibiotic range. Figure (3) shows the total number of occurrences documented in all veterinary units.

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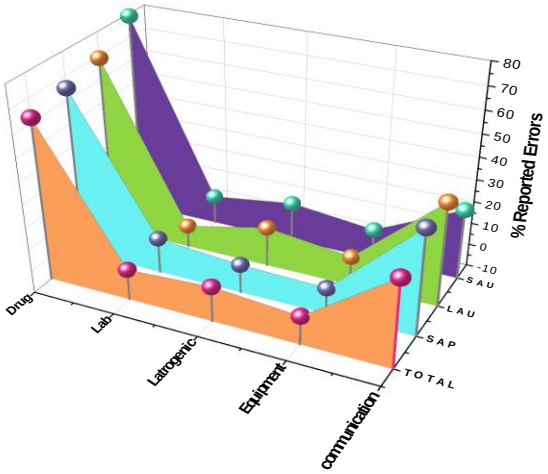

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Figure (3). Total number of occurrences documented in all veterinary (Source: Author)

Standards for the use of antibiotics in veterinary medicine

The recommendations for responsible Animal antimicrobial usage were formalized by the working group of chief veterinary executives in an effort to reduce the occurrence of prescription resistance to drugs. Veterinary professionals must adhere to the standards while giving antibiotics to animals to reduce the demand for these drugs. These criteria are the very minimum needs. The criteria are the standards of veterinary science that must be followed whenever antibiotics are used in animals and a living being is treated with compassion in accordance with applicable medication regulations (26). Only a veterinarian prescribes antibiotics and the animal owner administers them in accordance with stated directions while under the observation of the practitioner. Figure (4) shows the utilization of antibiotics in veterinary feed. To keep an eye on the effectiveness of the medication, the veterinarian has to verify this at appropriate intervals (27). Antibiotics should be used for treatment or metaphylaxis if the specific pathogen infecting the animal has been determined through appropriate and rigorous diagnostic processes to be antibiotic-sensitive. Antibodies and the pathogen's confirmation serve as the basis for the diagnosis.

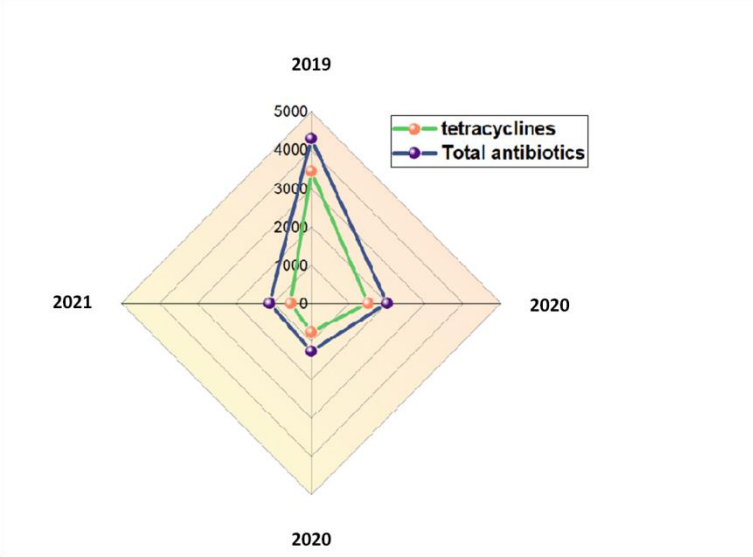

Figure (4). Utilization of antibiotics in veterinary feed (Source: Author)

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When changing to a different antibiotic, when using antibiotics in combinations that aren't fixed, or when using an antibiotic without following the directions on the label, a microbiological diagnostic is required on a regular basis in bigger animal herds if there is long-term or repetitive usage antibiotics must not be chosen from predetermined lists of first, second, or third option, according to the guidelines for responsible antibiotic use (28). Instead of using strict criteria, the selection process is centered on veterinarian excellence. The veterinarian has the exclusive responsibility of carefully choosing the best antibiotic.

- Antibacterials with strong tissue penetration that are reserved for extreme cases in human medicine (such as fluoroquinolones and third-generation cephalosporins) can be administered to a single animal under a stringent set of conditions when no other antibiotic works.
- Maximum potential margin of safety (dosage ratio between desirable and unfavorable effects); maximum possible narrowness of the antibacterial action spectrum.

The study's findings offer the first indications that veterinarians are following the recommendations for responsible antibiotic use; table (3) describes the period of antibiotic treatment, including medicinal feeding supplies, with improvements to their prescription practices to follow.

Table (3). Period of antibiotic treatment, including medicinal feeding supplies (Source: Author)

Treatment days							
Year	**Selected antibiotics**					**Total per animal**	**Total (106) a**
	Colistin ((5 mg/kg)	**Oxytetracycline (40 mg/kg)**	**Tilmicosin (10 mg/kg)**	**Tetracycline (20 mg/kg)**	**Chlortetracycline (30 mg/kg)**		
January 2019	741.6	39.8	78.5	634.5	1461	19.8	4.8
January 2020	674.3	10.8	67.3	811	232	13.7	2.10
March 2020	619.7	6.1	9.7	358.3	4311	31.7	8.3
March 2021	778.5	8.3	91.3	1059	251	19.8	4.8

Fewer prescriptions were written, a significant decrease in the number of treatment days, a shift away from prevention and toward expanded use of medicinal indication (from 80% in April 2019 to 95% in February 2021) and a shift away from earlier tetracyclines that were associated with a high incidence of improper dosage. No information is available regarding the usage of antibiotics by alternative modes of consumption throughout the monitoring period. Therefore, it is possible that injectables or other oral administration methods partially offset the decrease in antibiotic usage brought about by medicated feeding supplies. It was found at the end of February 2020, during the monitoring period and not long after the antibiotic guideline was published, that there was widespread antibiotic abuse in pigs in India. This sparked an intense discussion among the general public and the veterinary community about the more limited use of antibiotics in animals raised for food (29). This was made possible by a September 2021 amendment to restrict the maximum number of treatment days that veterinarians prescribe antibiotics to animals raised for food (30). The vet must reassess the animals to see if the antibiotic medication needs to be administered after that period. Table (4) shows medicated feedstuffs, including antibiotics utilized in vertical farming. Most people would agree that veterinarians were more likely to follow the recommendations for cautious antibiotic usage after hearing about the antibiotic controversy.

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Table (4). Medicated feedstuffs, including antibiotics utilized in vertical farming (Source: Author)

Year	Antibiotics														
	Colistin			Amoxicillin			Tilmicosin			Doxycycline			CTC		
	DDD			DDD			DDD			DDD			DDD		
April (2019)	48	14	42	30	28	46	0	34	68	0	100	0	0	34	42
January (2020)	89	12	4	42	36	28	0	0	100	0	0	0	0	0	0
All	62	16	26	42	36	28	0	22	82	0	100	0	0	30	23

DISCUSSION

A major contributor to the alarming rise in antibiotic resistance is the possibility of adverse effects from faulty veterinary medications, which endangers public health throughout the world. There has been a rise in antibiotic-resistant bacteria due to the widespread use of antibiotics in animal husbandry for illness prevention and growth promotion. Inadequate dosage and partial eradication of germs are more likely to occur when veterinary medications are flawed or poorly made. This can lead to the survival and spread of resistant strains and the possibility of animal transmission, wherein animals contract resistant germs and infect people. The vital role of responsible antibiotic usage in animal and human healthcare in curbing the rising threat of antibiotic resistance emphasizes the urgent need for rigorous regulations and immediate action to address the quality control of veterinary medications.

CONCLUSION

A major hazard to modern mankind is antibiotic resistance. Only by stepping up educational initiatives across various demographic groups can this trend be slowed down. Changes to established treatment procedures, clinical case discussions and the provision of extra teaching materials for staff members are important in medical organizations. The initial findings of tracking the use of antibiotics by livestock after the implementation of antibiotic regulations in India show that veterinarians are using antibiotics with more care when used on livestock. As a crucial risk management tool, these findings recommend mandatory recommendations for the responsible use of antibiotics in animals to minimize antibiotic consumption and the ensuing development of resistance. Assistance is thought to be required to encourage adherence to guidelines when it comes to animal care and to make them more effective. These include representative tracking of resistant bacteria and utilization, legally-based caps on the amount of antibiotics drugs that are supplied, given to livestock, basic controls as well as education for veterinarians, changes to antibiotic label instructions along with registration to meet rules and laws that are required in the pharmacy industry.

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