**Volume 4 Issue 1 Page: 0543 – 0553**



*Popular Article*

**Katyayini Sharma**  Shere Kashmir University of Agriculture &Technology Jammu India

> **Corresponding Author** Katyayini Sharma *neenabhardwaj@gmail.com Published: January 31, 2023*

*Antibiotics use in Livestock and its Linkages to Poisoned Food Cycle: Current Status and Way Forward*

**The phrase "antibiotics" refers to a broad category of chemical compounds produced naturally, semi-synthetically, and artificially, and used to prevent (bacteriostatic) or eradicate bacterial development (bactericidal). They are divided into two categories: narrow- and broad-spectrum antibiotics, depending on whether they have bactericidal or bacteriostatic properties. Additionally, the tetracyclines, aminoglycosides β-lactams, lincosamides, macrolides, pleuromutilins, and sulphonamides are among the classes of antibiotics that are more commonly used in agriculture globally and that are the subject of growing scientific concern with regard to their possible side effects and risk management strategies. As the years advance, the use of antibiotics is increasing at a rapid pace. The antibiotics are not only used for humans but for food animals too to promote growth and prevent infection. This improper use of antibiotics has an influence on the selection of microorganisms that are resistant to them. These bacteria, which are antibiotic-resistant, are spread from food animals to humans, milk, meat, soil, and water. The author reviews the extent of antibiotic worldwide and the mechanism by which the microorganisms develop resistant against the antibiotics. The spread of antibacterial resistant bacteria and mechanism of gene transfer from one bacteria to other has also been discussed. Preventive measures that can be taken to reduce the antibiotic use in food animals and reduce the antibiotic resistance in the mere future have also been highlighted.**

#### **WHY ARE ANTIBIOTIC USED IN LIVESTOCK**

The use of antibiotics in veterinary medicine began not long after they were first made available for the treatment of human infections. (Finley *et al*., *2013).*In the production of poultry, non-therapeutic antibiotic use has been particularly prevalent. Antibiotics are used in livestock production for many reasons such as i) therapeutically to alleviate disease symptoms, (ii) preventively to lessen bacterial pathogen infection in livestock animals under extremely stressful conditions, and (iii) as a growth promoter (Hayden, 2020). In order to cure mastitis in milking animals, penicillin was added to saline before the Second World War came to an end. In the following years, streptomycin, chloramphenicol, and several tetracycline formulations joined penicillin on the veterinarian's list. Since the early 1950s, antibiotics were added to animal diets, which became a new era of livestock management and meat production. Chlortetracycline was first utilised as a feed additive in 1950, and it still holds a sizable market share for feed antibiotics today. Other classes, such as quinolones, lincosamides and aminoglycosides are primarily used in disease treatment or prevention.The primary application of other classes, including quinolones, lincosamides, and aminoglycosides, is the treatment or prevention of disease. The most controversial category of antimicrobial use for the past many years has been its use as an animal feed additive (Milic *et al.,* 2013). In agriculture, almost 90% of antibiotics are administered as growth-promoting and preventative measures rather than for the treatment of infection. Low amounts of antibiotics added to high-energy feed for sheep, goats, and meat and dairy cattle increases the rate of weight gain and feed efficiency by 3% to 5%. Even in this modest dosage, the use of antibiotics promotes the development of microorganisms resistant to them (Timothy *et al.,* 2018).

# **EXTEND OF ANTIBIOTIC USE IN LIVESTOCK WORLDWIDE**

Antibiotics have been used for the purpose of livestock production for the past several years. In 1999, 20.5 million pounds of antibiotics were marketed for animal usage worldwide, according to the AHI. In that 17.7 million pounds were utilised for disease treatment and prevention, while 2.8 million were used to increase feed efficiency and growth. The top 5 nations with the highest consumption of antibiotics are: 1. China (23%) The United States  $(2%)$  Brazil  $(9%)$  3. 4. India  $(3%)$  Germany  $(3%)$ , 5. Compared to humans, livestock in the United States consumes 80% more antimicrobials annually (Mathew,2007).The estimated annual average consumption of antimicrobilas to produce One kg of beef, one kg of poultry, and one kg of pork requires 45 mg, 148 mg, and 172 mg of antimicrobials, respectively. According to the Organization for Economic Cooperation and Development (OECD), there will be a 67% increase in the number of antimicrobials used in livestock worldwide, which estimated around 63,151 tonnes in 2010 to 105,596 tonnes in 2030.India like all other countries also uses antimicrobials for therapeutics well as growth promotion in livestock(Feinmen,1998).There is currently a dearth of reliable information on the usage of antibiotics in livestock or the connection between animal-related resistant diseases and public health in India. According to a recent study, India, together with China, United States, Brazil, and Germany, accounted for 3% of the world's consumption of antibiotics used in livestock, swine, and bovine in 2010. By 2030, it is predicted that antibiotic use in animal feed will rise by 82% in India and by around twothirds globally.

# **BENEFITS AND PROBLEMS ARISING DUE TO ANTIBIOTIC USE**

Antibiotics in animal feed include advantages such as accelerating growth and efficiency, treating animals which are clinically sick and preventing or lowering the occurrence of infectious diseases. Increased efficiency, or the more effective conversion of feed into animal products, which results in an increase in growth rate, is by far the most common usage of antibiotics among these. Tetracycline and penicillin can significantly increase egg production, feed efficiency, and hatchability in chickens, but they have no impact on mortality. Penicillin, chlortetracycline, and oxytetracycline all exhibit enhanced growth rates but have minimal effects on mortality. Regular use of antibiotics in animal feed to promote growth and efficiency results in the survival of antibiotic-resistant bacterial strains. "Resistant" microorganisms are those that have evolved to evade the drug's effects. Antibiotic use directly contributes to the emergence and spread of resistance because these microbes multiply within the animal and spread to other animals. Then, as a result of these bacteria's growth, a significant number of bacteria develops antibiotic resistance. It is possible for bacteria that have developed resistance to one type of antibiotic to also develop resistance to similar drugs. These bacteria thrive in the animal's intestinal flora, and they can spread through contact with other animals' excrement and result in resistance in those animals. Consequently, once-easily-treatable infections seem to have become challenging or difficult to treat, leading to a significant rise in mortality rates and medical costs worldwide. Every time antibiotics are taken, perhaps to save a life or treat viral infections instead of bacterial infections, their useful lifespan and the lifespan of other medications of a similar nature are reduced. Typically, a significant subset of pathogen types account for a considerable percentage of resistance infectious diseases in humans. Some animal diseases are especially dangerous since they can spread quickly among species and trigger humans life-threatening infections. Methicillin-resistant Staphylococcus aureus (MRSA) is resistant to all ß-lactam antibiotics, including those belonging to the cephalosporin and penicillin groups. MRSA is known to be present in livestock, and when people come into contact with sick or infested animals, the bacteria can spread very quickly to humans. Since MRSAinfected animals frequently show no symptoms, it is possible for humans to contract LAMRSA without being aware of it. In densely populated low- and middle-income nations like India, where the incidence of contagious diseases is substantial and the capacity for health care is poor, the consequences of resistance infections are of particular concern. In addition to increasing mortality and morbidity resistant infections cost more to treat than sensitive ones because their frequently necessitate longer hospitalization and more expensive medications. Therefore, antibiotic resistance leads to higher rates of morbidity and mortality, negative side effects from alternative therapies, an increase in the spread of antibiotic-resistant bacteria and the infections they cause in the community, increased antibiotic use, a lack of medically efficient antibiotics, longer and more complex and difficult hospitalization, elevated cost of healthcare, and decreased sociocultural productivity.

#### **HOW ANTIBIOTIC RESISTANCE OCCURS IN THE ORGANISM**

An organism can acquire resistance in one of two ways: spontaneously or through acquisition. Some microorganisms have natural immunity, which exists because they lack key metabolic activities or target locations that make them susceptible to antimicrobial drugs. This is typically group-specific, such as the fact that penicillin has no effect on gramnegative organisms and tetracyclines have no effect on *Mycobacterium tuberculosis*. This type of resistance won't be producing any clinical problems (Magiorakos *et al.*, 2012).When an organism, which was previously sensitive, develops resistance as a result of using an antimicrobial agent over time, it is said to have acquired resistance (after an exposure).

## **THE BIOCHEMICAL ALTERATIONS IN DRUG OCCURS DUE TO THE FOLLOWING:**

**a) Alterations in the drug penetrations:** Decreased permeability of drug into the bacterial cell can occur due to change in bacterial cell permeability or altered transport system. It can also occur due to decreased porin size which allows the uptake of hydrophilic antimicrobials eg: aminoglycosides. Some resistance bacteria cause efflux of antimicrobial drugs which occurs due to the expression of P-Glycoprotein. This makes the cell resistant to various chemotherapeutic agents.

**b) Alteration in binding site:** Alteration in target site of organism can cause resistance as the drug will no longer be able to bind to the specific site. For example: alteration in protein binding site can cause resistance against penicillin it cannot bind to its target site. Alteration in 30S and 50S ribosomal subunit causes resistance to aminoglycosides and erythromycin.

**c) Alteration in metabolic pathway:** Alteration in metabolic pathway causes resistance to the antimicrobial by bypassing the reactions inhibited by the antimicrobials. Folic acid is essential for the survival of both mammalian and microbial cells. Folic acid transporter protein is present in mammalian cell membrane but is absent in bacterial cell membrane therefore bacterial cell require paraaminobenzoic acid (PABA) for the synthesis of folic acid. Sulfonamides act by blocking or inhibiting this folic acid metabolic pathway. Sulfonamide resistant bacteria do not need PABA as they synthesis their own PABA, a key metabolic intermediate involved in synthesis of folic acid and thereby showing resistance to sulfonamides.

**d) Drug inactivating enzymes:** The microbes also develop resistance by producing drug inactivating enzymes which destroy the antimicrobial agents. For example: bacterial cells that synthesis beta lactamase destroy penicillin and other cephalosporins by cleaving the beta lactam ring. Chloramphenicol is inactivated by acetyltransferase enzyme and aminoglycosides by transferases.

**e) Cross resistance:** It is a kind of acquired resistance in which bacteria resistant to one antimicrobial agent also becomes resistant to other related antimicrobial agent without having exposed to the later. In two way cross resistance the bacteria resistant to one antimicrobial agent are also resistant to the other and vise versa. For example: cross resistance between neomycin and kanamycin. The bacteria resistant to neomycin will also be resistant to kanamycin and the bacteria resistant to kanamycin will also be resistant to neomycin. Whereas in partial cross resistance the bacteria resistant to one antimicrobial agent will be resistant to the other but vise versa will not occur. For example: bacteria resistant to gentamycin will be resistance to kanamycin and streptomycin but the bacteria resistant to kanamycin and streptomycin will not necessarily show resistance to gentamycin.

**f) Biofilm formation:** An extracellular polymeric material matrix during biofilm formation allows for the development of antibiotic resistance. The matrix's negative charge prevents antibiotics from establishing an impact on the bacteria. Antibiotic activity is rendered inactive by covalent modification of antibiotics by matrix-based enzymes.

**MECHANISM OF ANTIBIOTIC RESISTANT GENE TRANSFER IN THE ENVIRONMENT**

Any gene, including antibiotic resistance genes, has the potential to be passed across bacteria in the procedure outlined below (George, 1998). Another concern is whether or not the receiving bacterium's DNA will incorporate the transmitted genes. A bacteria can get harmed by foreign DNA, hence there are systems in place that break down incoming DNA. These systems are not, however, entirely effective. The likelihood of maintaining the incoming DNA increases if it is absorbed and benefits the bacteria. For instance, if a bacteria acquires an antibiotic resistance gene and then is exposed to the antibiotic, it will fare better than susceptible neighbours and can proliferate. Genes for antibiotic resistance can be transferred in three different ways:

**1. Conjugation:** Conjugation is the transfer of DNA, such as chromosomal and plasmid DNA, from a donor to a recipient cell. With the aid of pilli, conjugation necessitates direct physical cell-to-cell contact between the donor and receiver. Because conjugation requires direct cell contact, cell densities and the environment in which the bacteria reside have a significant impact on how frequently conjugation occurs. For instance, huge bacterial populations that coexist in close proximity to one another in moist habitats such as the gastrointestinal tracts and biofilms frequently undergo conjugation events. In general, it is believed that conjugative mechanisms of gene transfer in the environment play a significant role in the spread of genetic information. These mechanisms affect a wide variety of genera and species, and they are thought to be responsible for the occurrences of similar DNA sequences among diverse bacterial species. When a conjugative plasmid is transferred from a parent cell to a recipient that also has a non-conjugative plasmid, and then both plasmids are delivered to a recipient that contains neither plasmid, triparentalmobilisation of DNA can occur. Several genes for antibiotic resistance are found on mobile genetic elements like plasmids, transposons, or integrons and are easily passed between bacteria of the same species as well as between bacteria belonging to other genera. The ability of environmental relevant concentrations to promote plasmid transfer in uncontrolled natural situations is not fully understood. Due to the high levels of bacteria in manure and the possibility for long-term survival of introduced bacteria, conjugation events may be particularly frequent throughout the phases of waste storage and in the early days just after land application. The scale of conjugation is yet unknown, despite being the most common lateral gene transfer technique among commensal soil bacteria (Enne, 2005).



**Figure 1. Transfer of antibiotic resistant gene by conjugation process with the help of sex pilli**

**2. Transduction:** Bacteriophages can operate as a conduit for the transfer of DNA between bacterial cells, a process known as transduction. In generalised transduction, DNA from any portion of the host bacterial genome is wrongly packed during replication into a phage capsid (protein coat), and upon infection of a new host, the foreign DNA may be inserted into the host chromosome through homologous recombination. Direct inheritance is possible when the DNA is a replicon, such as in plasmids. The retention and expression of genetic determinants may take place once the foreign DNA has been inserted into the host bacteria. Bacteriophages are relatively prevalent in all natural habitats, and transduction is now regarded to be more important than previously assumed in the evolution of bacteria. As was already indicated, phage function is thought to be vital for microbial ecology. Over the

past 20 years, it has been demonstrated that transduction occurs in a range of contexts, including sewage treatment plants and natural systems such wetlands, marine, lake, and stream sediments and waters. Although there is still much to learn about the prevalence of phages and natural transduction in soil, recent research has indicated that transduction may be an important gene-transfer mechanism in soil systems (Kapoor and Saigal, 2017).



**Figure 2. Transfer of antibiotic resistant gene viabacteriophage through transduction**

**3. Transformation:** Bacteria can change naturally to acquire new genetic information this process is known as transformation. This process requires particular host genes to transport exogenous DNA molecules into the cell cytoplasm and to stabilise the integration of the transforming DNA into the recipient genome. Cells must be genetically competent or in a condition that allows for the binding and import of foreign DNA in a form resistant to intracellular restriction nucleases. There have been several reports of naturally competent bacteria, including several genera that are found in soil. Gram-positive and gram-negative bacteria, including those from the genera Bacillus, Micrococcus, Agrobacterium, Pseudomonas, and Vibrio, to name a few, present in natural habitats, have both been proven to possess the potential to naturally transform. It has been demonstrated that some bacteria's competence factors can also make other cells competent. For instance, in a soil microcosm investigation, cell lysates of the bacteria Acinetobacter sp., Pseudomonas fluorescens, and Burkholderiacepacia naturally transformed the strain BD413 of Acinetobacter sp., with the activity decreasing by 31% after one hour in nonsterile soil. A similar investigation discovered that the transformation of Acinetobacter sp. strain BD413 was also stimulated by plant exudates in the soil rhizosphere. While not all bacteria can transform naturally, many more species can be altered intentionally in the lab artificially. Artificial transformation, which is different from the active process of natural transformation, as it employs chemical (CaCl2) or electrical (electroporation) procedures to modify the cell membrane and allow passive absorption of DNA. Although studies have shown that natural salt (Ca2+) concentrations in freshwater and soil, as well as lightning occurrences, may generate competence in bacteria, natural transformation has traditionally been assumed to be more relevant in situ. The stability and bioavailability of free DNA is a crucial element for transformation processes in nature. Although DNA has been demonstrated to sorb to sand, the clay fraction is the main component that sorbs DNA in soil systems. DNA from both chromosomes and plasmids may bind to clay particles, especially when the pH is neutral or lower and when there are plenty of multivalent cations present. However, multiple studies

have shown that DNA adsorbed to surface active particles in soils is protected against nuclease activity, suggesting that the durability of naked DNA in soil environments and the retention of its capacity to change cells have not been well examined. The probability of native soil bacteria acquiring additional genetic material, including genes that confer antibiotic resistances, would be suggested by the chance of DNA remaining in soil, particularly ones richer in coarse clays and humic acids.



**Figure 3. The transfer of an antibiotic-resistant gene from one bacterial strain to another by the process of transformation. Dead bacteria's exogenous DNA is fragmented and taken up by living bacteria from their environment, where it is then integrated into their DNA.**

## **HOW ANTIBIOTICS TRAVEL FROM LIVESTOCK TO FOOD CYCLE**

Antibiotic residues, antibiotic-resistant bacteria, and resistance genes are all regarded as environmental contaminants that are to blame for the persistent public health catastrophe that exists around the globe (Xi *et al.,* 2009).Many antimicrobial classes that are used for people are also utilised on animals raised for food. In addition to using these medications to treat sick animals, many food animal producers also use them to encourage development or prevent common illnesses in crowded, unhygienic industrial workplaces. The major cause of the emergence of antibiotic-resistant bacteria, which then spread into populations due to the indiscriminate use of antibiotics Workers at farms, slaughterhouses, and veterinary clinics who have frequent contact with colonised or diseased animals run the danger of harbouring these resistant bacteria and spreading them to others. The primary source of bacteria and antibiotic residues entering the environment from food animal production is manure, which affects both the environment's bacteria and the bacteria in wild fauna. The excretion of waste by grazing animals, the air dispersion of feed, and the inhalation of antibiotic-containing manure dust are additional possible avenues for antibiotic residues to reach the environment. Many antibiotics are not totally absorbed in the gut, which causes the parent substance and its breakdown products to be excreted. According to estimates, up to 75% of the antibiotics given to animals in feedlots might be excreted into the environment. Approximately 25% of the oral dosage of tetracycline was also shown to be eliminated in faeces, and another 50% to 60% was discovered to be excreted in urine either unaltered or as an active metabolite. The technique of applying animal dung to the ground on a broad scale allows for the environmental introduction of antibiotics (Boxall, 2004).Once the antibiotics have been discharged into the environment, they can move into surface- and groundwater either as a dissolved phase or as adsorbed to colloids or soil particles. Significant levels of antibiotics may be present in manure and waste slurries, and their

presence in soil might endure after land application (Manyi-LoChristy, 2018). Bacteria and viruses have the huge ability to spread deeply into the subsurface environment and can even permeate and reach limited aquifers as hosts of genetic elements that might include genes for antibiotic resistance. Bacterial activity and migration into groundwater in the soil after manure application have been discovered in several investigations. According to a research of the vadose zone at manure application locations, the amount of water in the manure was directly related to the amount of faecal bacteria that were delivered deep into the soil. The researchers reached the conclusion that applying animal dung to soil can easily result in the contamination of groundwater with faecal bacteria, especially when the soil is damp. They also found that macropores, but not total porosity, are crucial for the movement of bacteria through soil (Joanne, 2009).When such water or manure is used on crops, it also contaminates the crops. Additionally, these crops that are tainted with bacteria resistant to antibiotics can now spread those bacteria to people, causing people to develop antibiotic resistance (Xi *et al.,* 2009).Humans develop resistant infections when exposed to these animal-transmitted, antibiotic-resistant microorganisms. The uses of antibiotics in animals as well as the development of bacteria linked to antibiotic resistance in humans are connected, according to several researches. Antibiotics kill bacteria that are sensitive to them, while resistant microorganisms are allowed to proliferate and flourish. When raw ingredients are polluted or cross-infected with other foods and the environment during preparation, resistant bacteria can spread to animal flesh, contaminate eggs via animal faeces, and reach humans through undercooked or raw food. There have been reports of antimicrobial residues in milk. Mastitis is one of the most frequent clinical problems seen in dairy farms, and it has been found that the disease-affected cows' and buffaloes' milk contains bacteria that have a wide range of resistance against commonly used antibiotics. Animals with mastitis have occasionally been shown to co-infect with several drug-resistant bacteria (Timothy *et al.,* 2018).



**Figure 4. Illustration of antibiotic use and movement in food cycle**

#### **FUTURE IMPLICATIONS AND WAY FORWARD**

The efficacy of antibiotics against diseases in animals and subsequently in humans declines when they are administered to animals for whatever reason. Some applications, such the treatment of bacterial infections in animals, are acceptable. However, it is superfluous and avoidable to use antibiotics merely as growth promoters and for some preventive purposes. The goal of these guidelines is to minimise the quantity of antibiotics used in livestock overall without endangering the health of human or animals. The following ideas are advised in order to preserve antibiotic efficacy in both humans and animals.

1) Maintaining a national surveillance and monitoring system to track the usage, resistance, and residues of veterinary antibiotics. In India, there has been no comprehensive tracking of the usage, residues, and resistance of veterinary antibiotics. A sentinel monitoring system should be established to address this knowledge gap, gathering qualitative (*i.e.,* patterns of use) and quantitative data to monitor patterns of use and levels of resistance over time. The system may be created and implemented by a working team composed of veterinary scientists, ministry officials, and surveillance experts. Determining the implementation partners as well as the bacteria and drugs that will be a part of the surveillance programme are primary steps.

2) There is a need to create incentives that will lower antibiotic use without endangering the health of people or animals. Refrain from giving animals unwanted antibiotics. Randomized intervention trials can shed more light on the kinds of incentives that may be effective at lowering usage. Trials may, for instance, examine the effects of funding microbiological tests for bacterial infections in animals, establishing national certifications for animal food items sold for human consumption that are free of antibiotics, or introducing alternative disease control strategies.

3) Prevention of animal illness and infection can also result in a decrease in antibiotic usage overall. This may be accomplished by maintaining a suitable level of environmental cleanliness for animals, enhancing the quality of the food, and breeding cattle with genetic resistance to disease.

4) Educate farmers, veterinarians, and consumers on the risks posed by antibiotic resistance. Antibiotic resistance is still largely unknown on a global scale. Animal antibiotic usage can be decreased by education and public awareness campaigns aimed at farmers, veterinarians, and the general public. Farmers might be contacted on market days and fairs, via extension education provided by veterinary and agricultural universities, as well as through radio, television, and print advertisements (Finley *et al.,* 2013).Veterinarians may be taught by adding lessons on antibiotic resistance to college curriculum, increased demand for items without antibiotics may be brought about by boosting public awareness through traditional and social media.

5) Accurate illness and pathogen detection is necessary in order to choose an antibiotic that is particularly effective against that infection. It leads to reduction of repeated trial and error batteries of antibiotics. Viral illnesses should not be mistaken with bacterial infections, and the pathogen shouldn't be resistant to the antibiotic of choice.

6) Gradually ending the sub therapeutic use of antibiotics in animals. Antibiotic usage and resistance might be drastically decreased if sub therapeutic use of antibiotics gets vanished. With monitoring to make sure that the phase-out does not have unforeseen negative effects on animal health and that total antibiotic use does reduce, this use should be gradually

phased out. It is important to keep track of the overall antibiotic usage and manufacturing expenses. Adoption of antibiotic substitutes along with other rewards as suggested above may support the progressive phase-out of sub therapeutic antibiotic usage while maintaining animal health.

7) Vaccinating animals properly is another approach to prevent illness and cut back on antibiotic use. When it comes to the prevention of some animal diseases, vaccination can be a trustworthy alternative to medicine use. Oral administration of attenuated live vaccines has a number of benefits over injected vaccines. Needles are not necessary, and animals do not need to be handled individually, as the vaccination is often administered by spray or in drinking water. Additionally, because certain live vaccines penetrate and activate the gutassociated lymphoid tissue, they can produce humoral, cellular, and mucosal immune responses depending on the parent pathogen's life cycle.

8) It's crucial to administer the antibiotics to the animal as directed by the veterinarian. The most frequent mistake made by farmers or owners is missing doses of prescription antibiotics or administering antibiotics to other animals without consulting a veterinarian, both of which can result in antibiotic resistance.

9) Following simple food safety tips: COOK, CLEAN, CHILL, SEPARATE can reduce the chances of infection-

 COOK-Food needs to be ookedc till the inside temperature is safe. Whole beef, pig, lamb, and veal should be cooked at 68°C (and given three minutes to rest before chopping or eating), whereas ground meats should be cooked at 72°C and all poultry, including ground chicken and ground, must be cooked at 74°C.

 CLEAN-Hands should always be washed before handling raw foods to prevent contamination, particularly after coming into touch with animals or an animal habitat. When handling raw poultry, fish, or meat, wash your hands immediately. Before and after cooking, wash the grill, cutting boards, and work surfaces.

 CHILL-Foods should be refrigerated within two hours of cooking and should be kept in the freezer below 4°C.

 SEPARATE-Raw meat, poultry, fish, and eggs may transfer bacteria to prepared dishes. Store cooked and uncooked food separately. Handle prepared meals and raw meats separately. Use different cutting boards to prepare raw meats and any food that will be eaten without cooking.

## **CONCLUSION**

Antibiotics resistance is not a simple relationship between cause and effect but a complex of biological and ecological interactions. Although the use of antibiotics becomes necessary in treating and preventing infections in veterinary practice but its excessive use such as in growth enhancers and sub therapeutic measures should be avoided. Multifaceted and complete strategies, as enlisted by the WHO Global Action Plan and FAO Action Plan in check with the One Health approach should be used to prevent the transmission of antibiotic resistance and infectious diseases from farm-to-fork, avoid potential pandemic situations and preserve the efficacy of antibiotics to assure food safety, food security and global health.

## **REFERENCES**

Boxall, ABA, Fogg LA, Blackwell PA, Kay P, Pemberton EJ and CroxfordA (2004) Veterinary medicines in the environment. *Rev. Enviro. ContamToxicol* 180:1–91.

Enne, VI, Delsol A A, Davis GR, Hayward SL, Roe JM, and Bennett PM (2005) Assessment of the fi tness impacts on Escherichia coli of acquisition of antibiotic resistance genes encoded by different types of genetic element. *J AntimicroChemother*56:544–551.

FeinmenSE(1998)Antibiotics in animal feed: drug resistance revisited. *AmSocMicrobiolNews* 64:24-30.

Finley RL, Collignon P, JoakimLarsson DG, McEwen SA, Xian-Zhi L, Gaze WH, Reid-Smith R, Timinouni M, Graham DW, Topp E(2013) The Scourge of Antibiotic Resistance: The Important Role of the Environment. *Clin Infect. Dis.* :57:704–710. doi: 10.1093/cid/cit355.

George G, (1998) Agricultural use of antibiotics and the evolution and transfer of antibioticresistant bacteria. *Canadian Med. Assoc. J* 159:1129-36.

Hayden D, Hedman Karla A, Vasco Lixin Zhang(2020) A Review of Antimicrobial Resistance in Poultry Farming within Low-Resource Settings. Libretexts. *Bacterial Transformatio*n.4.1.

Joanne C, Chee-Sanford,Roderick I, Mackie and Satoshi Koike.van G. Krapac.Yu-Feng Lin, Anthony C(2009) Transport of Antibiotic Residues and Antibiotic Resistance Genes following Land Application of Manure Waste. *J Environ Qual* 38:1086–1108

KapoorGarimaand SaigalSaurabh(2017) Ashok Elongavan. Action and resistance mechanisms of antibiotics: A guide for clinicians.pp116.

Magiorakos A, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, GiskeCG(2012) Multidrugresistant, extensively drug-resistant and pandrug-resistant bacteria: an internatiojnal expert proposal for interim standard definitions for acquired resistance. *ClinMicrobiol Infect* 18(3):268–81.

Manyi-LoChristy h, MamphweliS ampson, Meyer Edson and Okoh (2018) Antibiotic Use in Agriculture and Its Consequential Resistance in Environmental Sources: Potential Public Health Implications. Published online Mar 30. doi: 10.3390/molecules23040795

Mathew G Alan 1, IsselRobin C, LiamthongS(2007) Antibiotic resistance in bacteria associated with food animals: a United States perspective of livestock production. *Summer* 4(2):115-33. doi: 10.1089/fpd.2006.0066.

Milic N, Milanovic M, Letic NG, Sekulic MT, Radonic J, Mihajlovic I, Miloradov V(2013) Occurrence of antibiotics as emerging contaminant substances in the aquatic environment. *Int. J Environ Health Res* 23:296–310.

Timothy F Landers, Bevin Cohen, Thomas EWittum and Elaine L Larson(2018) A Review of Antibiotic Use in Food Animals: Perspective, Policy, and Potential . *Molecules :* 23(4): 795.

Xi C, Zhang Y, Marrs CF, Ye W, Simon C, Foxman B, Nriagu J(2009)Prevalence of antibiotic resistance in drinking water treatment and distribution systems*.Appl.Environ .Microbiol*. : 75(17):5714-8.