CFAES SCHOOL OF ENVIRONMENT AND NATRUAL RESOURCES

Haphazard Use of Antibiotics & Antibiotic Resistance Manifestations in the Food Chain

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INTRODUCTION

Antibiotic resistance is the process in which fungi or bacteria gain the ability to tolerate toxic influence, adapt, and proliferate in the presence of antibiotics. Antibiotic resistance poses a threat to human and animal health and challenges the agricultural food supply and the integrity of the environment worldwide. Relentless continued use and misuse of antibiotics created a continuum for perpetuating horizontal and vertical evolution of antibiotic resistant bacteria proliferating in unfavorable environments of newer and more antibiotics. This continuum makes classification required to document all antibiotic resistance threats not be feasible. Although antibiotics are a utilitarian part of modern medicine for nearly a century, their efficacy and safety do not meet the demands of the growing population facing the global threat of antibiotic-resistant infectious diseases. Similar challenge encounters intensifying animal production. The complex global antibiotic resistance phenomena required innovative multilayered interdisciplinary solutions. Four major strategic directions are: 1) utilizing immune response with immune therapies, antibodies and plant-based metabolites, stimulating immunity along with antibiotic effects; 2) developing physical devices, including hemofiltration devices; 3) antimicrobial adjuvants (AA) and nitric oxide-based nanotherapies disrupting bacterial pathways; and 4) ecosystem-influenced methods, utilizing predatory bacteria, bacteriophage, transplantation of fecal microbiota, and quorum sensing inhibitors, intercepting bacterial communication. Combating the global spread of antibiotic resistance also requires comprehensive and incessant efforts of policymakers in agriculture working with experts in diverse fields of microbiology, biochemistry, clinical research, genetic and computational engineering.

Figure 1. Schematics of major facilitations for antibiotic resistant genes (ARG)

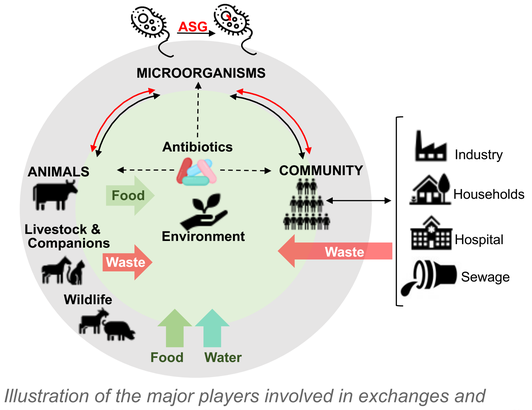


Illustration of the major players involved in exchanges and interaction with both antibiotics and the environment surrounding them to signify the transmission paths in which bacteria are able to develop ARG mutations.

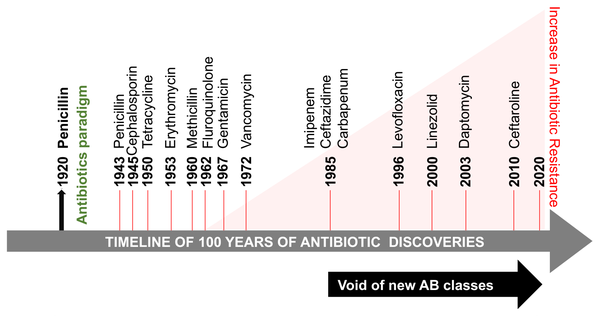
METHODS & ANALYSIS

The method for this study is an analysis of pathways that were previously published. In order to justify the comprehensive and educative nature of this review over two hundred sources were used to build a strong foundation from collection, analyses, and interpretation of both qualitative and quantitative data.

MAJOR FINDINGS

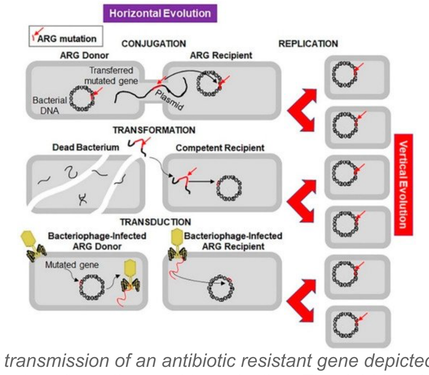
The completed and published review paper highlights many important aspects with regards to nutrition and the environment. Four major aspects of the review that are ideal for discussion would be the void in antibiotics discovery, evolution of antibiotic resistance, antibiotic uses, and others.

Figure 2. Timeline of antibiotic discovery and its onset resistance



This figures depicts three major details to note; the beginning of antibiotics development, followed by the discovery of penicillin there is a surge of antibiotics discovery between 60's and 80's, decline in antibiotics development between late 80's and 90's, and the void in new antibiotics classifications.

Figure 3. Mechanisms of horizontal and vertical transmission in bacteria



Horizontal transmission of an antibiotic resistant gene depicted by conjugation, transformation, and transduction. The right-hand side of the figure shows the vertical evolution carried out by bacteria replication containing the ARG.

Table 1. Mechanism of action of antibiotics

Mechanism of Action	Name of Antibiotic Families
Inhibition of protein synthesis	Tetracyclines, aminoglycosides, streptogramins, ketolides, macrolides, lincosamides, daptomycin
Inhibition of DNA synthesis	Fluoroquinolones, daptomycin
Inhibition of RNA synthesis	Rifampin and other metronidazoles, daptomycin
Inhibition of cell wall synthesis	Penicillins, cephalosporins, carbapenems, monobactams, glycopeptides
Disrupt functions of bacterial outer membrane	Daptomycin, polymyxin B, colistin, and lipopetides
Competitive inhibition of folic acid synthesis	Sulfonamides, trimethoprim

This table contains antibiotics that are routinely prescribed to patients. Even though they have been tested for their efficacy and benefits, the haphazard uses are underestimated, hence the debilitating effects caused antibiotics in humans are often condoned. For instance, fluoroquinolones are routinely prescribed worldwide, even though they cause several side effects, encompassing damage to muscles, tendons, neuropsychiatric disorders, and mitochondrial toxicity.

Table 2. Antibiotic resistant genes (ARG) in animal production settings

Sl. No.	Bacterial Species	Infection	Antibiotic Resistance Pattern	Sources of Human Infection	Genes
1	*Campylobacter* spp.	Gastrointestinal sequelae: Guillain-Barré syndrome	Fluoroquinolones, erythromycin	Food-producing animals (poultry)	*tetO, gyrA*
2	*Enterococcus* spp.	Sepsis, urinary tract	Aminoglycosides ampicillin vancomycin	Food-producing animals (poultry); People exposed to hospital care, food animals	*Tuf, VanC-1, VanC-2-VanC-3, pbp5*
3	*E. coli*	Gastrointestinal, urinary tract, diarrhoea	Quinolones sulphonamides trimethoprim	Childcare facilities	*Bla, qnrS, frdD*
4	*Salmonella* spp. (non-typhoidal)	Gastrointestinal, diarrhoea	Cephalosporins quinolones tetracyclines	Food-producing animals (pigs, cows, poultry)	*IntI1, qnrA*
5	*S. pneumoniae*	Otitis media, pneumonia, sinusitis, meningitis	Penicillin, macrolides, cephalosporins, tetracyclines	Childcare facilities, paediatric populations	*ermB), mef*
6	*S. pyogenes*	Pharyngitis, impetigo, cellulitis	Macrolides, tetracyclines	Childcare facilities, paediatric Populations, schools	*ermB, ermA and mefA*
7	*S. aureus*				
	Community-associated	Skin, soft tissue, pneumonia, sepsis	Methicillin, cephalosporins, macrolides	Childcare facilities, injections, drug users	*ermA), ermC), tetK, tetM, aacA-aphD, vatA), vatB) and vatC)*
	Healthcare-associated	Endocarditis, pneumonia, sepsis	Methicillin, cephalosporins, quinolones, aminoglycosides, macrolides	People exposed to healthcare facilities such as nursing homes, dialysis, recent surgery or hospitalization	
8	*N. gonorrhoeae*	Urethritis, pelvic inflammatory disease	Penicillin, cephalosporins, quinolones	Commercial sex workers	*penA, penB, NorM*

This table illustrates the bacteria present, how it is introduced to humans for infections, and the use of antimicrobial substances in animal production for food.

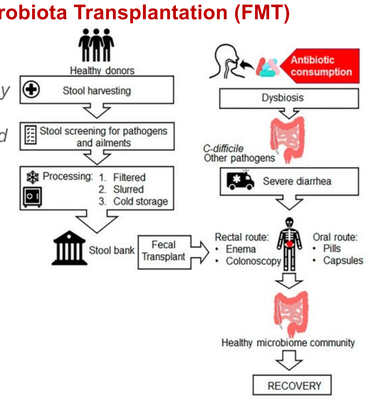
These findings are significant, especially with the context of an overall 176% increase in antibiotic use was observed during the decade 2000–2010 in Brazil, Russia, India, China, and South Africa (BRICS). Continuing on this point, animal consumption of antimicrobials in BRICS countries is expected to increase up to 199% by 2030 compared to current use. In human populations its expected growth will be around 113% during the same period. Moreover, with respect to figure 1, it begs to scrutinize the various environments that bacteria can penetrate, interact, proliferate by spreading, and building antibiotic resistance among both animals and humans. In order to mitigate and combat infectious pathogens containing ARG, there are several mediations that are being explored and implemented.

DISCUSSION

There are many emerging therapies and prospective strategies that are being explored or implemented. Some of which will be discussed below.

Figure 4. Faecal Microbiota Transplantation (FMT)

Depiction of sample preparation where stool is harvested from healthy donors, processed via different stages, followed by cold storage in stool bank. Processed faecal microbiota of healthy donor stored in stool bank is either delivered via rectal route or oral route to the diseased patients (recipient) to provide a healthy microbiome community.



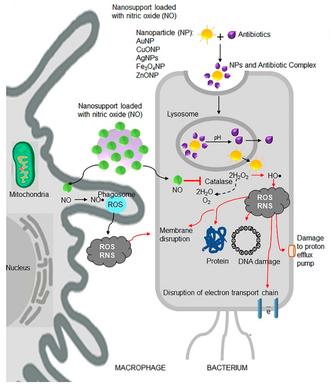


Figure 5. Nanoantibiotics

Principle of action by nano-antibiotic therapies including nitric oxide (NO) releasing nanoparticles and nanoparticles in combination with antibiotics is illustrated. In bacteria, NO leads to the production of harmful ROS and reactive nitrogen species (RNS) which are responsible for oxidative and nitrosative stress and death of bacteria.

Bacteriophage therapy, predatory bacteria, immunotherapeutics, haemofiltration devices, quorum sensing inhibitors, antimicrobial adjuvants, antimicrobial peptides (AMPs) or bacteriocins, essential oils, RNA therapy, and use of vaccines, are some of the other prospective strategies.

CONCLUSION

Antibiotics became a part of modern medicine around seven decades ago and their efficacy and safety do not meet the demands of the intensifying animal production and growing human population, facing the global threat of infectious diseases. Experts from diverse fields such as clinical research, microbiology, genetic and computational engineering, imaging and modelling should work jointly to evolve strategies and develop novel therapeutics to address this problem.

BIBLIOGRAPHY

Kumar SB, Arnipalli SR, Ziouzenkova O. Antibiotics in Food Chain: The Consequences for Antibiotic Resistance. Antibiotics. 2020; 9(10):688.