

Environmental and Public Health Risks Associated with Antibiotic Resistance Genes (ARGs) Spread in Environment: A Comprehensive Review

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ABSTRACT

Currently, the use of life saving antibiotics is growing up rapidly due to its multi-effectiveness for curing from bacterial infected diseases. If same antibiotics are frequently consumed, then it kills – susceptible bacteria but leaves resistance gene. Thus, some bacteria obtain resistance capacity against some antibiotics called antibiotic resistance bacteria (ARBs). Consequently, uncontrolled production and unmonitored consumption of antibiotics is responsible for – antibiotic resistance genes (ARGs) spread in environment. Hence, it is considered as emerging contaminants posing a potential worldwide human health risk, but mass people aren't concerned about it hereto. Therefore, we conducted this review to explore the already performed researches on this topic and their gaps. It revealed that researchers have already detected – wastewater, surface water, wastewater treatment plant, sludge, landfill leachate, soil, animal washed lagoon, and animal farm as reservoir of ARGs. China is the largest producer and consumers of antibiotics, followed by U.S. in the world wherein (46.1%) are used in livestock's industries. Consequently, intensive animal husbandry is declared as-hotspot of ARGs. But, little knowledge is known about the associated risks with ARGs. However, 149 unique ARGs are detected from swine farm in China by researchers. Still, there is no universal technology to remove or kill ARGs from such sources but – advanced technologies are performing better.

Keywords: Antibiotics; Resistance; ARBs; ARGs; Environment; Health; Contamination.

I. INTRODUCTION

Antibiotic drugs have reduced the burden of common infectious diseases and have become essential for many medical interventions [133, 65]. It is a class of naturally occurring and synthetic chemical compounds with antimicrobial activity that are widely used – in human and veterinary medicine. They are applied in the treatment and prevention of bacterial infection which may either kill or inhibit the growth of bacteria. In contrast, antibiotic resistant pathogens have emerged and spread amidst – human and animal populations [34, 55, 28]. The increasing incidence of resistance to a wide range of antibiotic agents, by a variety of organisms is a major concern facing modern medicine. Therefore, a major problem has been arisen due to infectious diseases caused by resistant bacteria that are related to – high

mortality and healthcare costs [16]. On the other hand, *antibiotic Resistance* (AR) is a natural phenomenon and it occurs when an antibiotic has lost its ability to effectively control or kill bacterial growth [134]. Genetically, AR spreads through two ways of – bacteria populations, such as, new generations inherit and bacteria share or exchange sections of genetic material with other bacteria [11]. When an antibiotic is used, bacteria that can resist that antibiotic have a greater chance of survival than those are – 'susceptible.' These bacteria are known as *Antibiotic resistant bacteria* (ARB) which can't be controlled or killed by antibiotics; rather they can survive and even – multiply in the presence of an antibiotic viz. *Staphylococcus aureus* [75]. Besides, some resistance occurs without human action, as bacteria can produce and use antibiotics against other bacteria. However, bacteria may also become resistant in

two ways, such as, by a genetic mutation and by acquiring resistance from another bacterium [106]. Consequently, *antibiotic resistance genes (ARGs)* are emerging contaminants posing a potential worldwide – human health risk. Wastewater, intensive animal husbandry and animal manure are believed to be a major contributor of ARGs into environment. Hence, swine farms are declared as – hotspots for pervasive and abundant ARGs in China [17].

However, *antibiotics* revolutionized in medicine in the 20th century, and together with vaccination led to the near eradication of diseases, such as, tuberculosis in the developed world. Since, World War II, many more antibiotics isolated from – fungi and bacteria, which have been used to treat a wide range of human and animal infections [69, 136, 6]. An increase in the frequency of antibiotic resistance in bacteria, since the 1950s has been observed for all major classes of antibiotics used to treat a wide variety of diseases [101, 28]. But the loss of efficacy of antibiotics against common pathogens, has not only led to a shift towards more – expensive antibiotic drugs in high-income countries, but also to increased morbidity and mortality in low-income and middle-income countries [41]. To predict risk of antibiotics, identification of spatial and temporal trends in antibiotic consumption is important to understand the epidemiology of AR [37]. The quantity of antibiotic drug consumption is – a major driver of AR and variations across the country, wherein its consumption varied significantly with season in many countries. It was found that between 2000 and 2010, consumption of antibiotic drugs increased by (36%) while in Brazil, Russia, India, China, and South Africa accounted for (76%) of this increase [10]. Besides, Alexander Fleming famously warned that the ignorant may someday misuse his – life-saving discovery *penicillin* and select for resistant bacteria. According to Van-Boeckel et al. [126], the proliferation of ignorance is only poised to increase. Based on global datasets of veterinary antibiotic use, it was estimated that from 2010 to 2030 antibiotic use in food-animal production will increase by (67%) [98]. On the contrary, it is well known that multiple human-made chemicals, when entering into environment, will disperse over much wider distances and persist for much longer than initially anticipated and envisioned. The production, use and disposal of the different chemicals employed in common – households, agriculture, industry, and for medical

purposes are expected to grow rather than stabilize, while the long-term effects of chemical pollution of surface and groundwater's are largely unknown. Micro-pollutants are sometimes also referred to as micro-constituents or pharmaceutical and personal care products (PCPs) [102]. Anyhow, through different ways antibiotics and ARGs are spreading in environment, for example – water, soil, and food which ultimately entering into human body unconsciously.

Globally, the antibiotics production and application in diverse fields are rapidly accelerating, especially in China, USA, EU, India, Russia and Brazil [124, 19, 66, 10]. But its long term environmental impacts and associated health risks are still unknown to mass people due to its – silent emerging approach. Though several studies have already been done in limited countries but little knowledge is informed hereto. Hence, the absence of sufficient studies on ARGs has redoubled the problems. Therefore, we conducted this study to explore and gather all related published data as well as to detect research gaps so that it can facilitate future researchers to perform further study.

II. REVIEW FINDINGS

Global Scenario of Antibiotics Consumption

Life-saving antibiotic drugs have become inevitable for medical interventions, meanwhile, antibiotic-resistant pathogens have emerged and spread worldwide [65, 66, 133]. Currently, such pathogens have become a global problem because it has increased the cost of life saving antibiotics [87, 44]. The emergence of drug-resistant bacterial strains is due to the selection pressure imposed by use of antibiotics. Identification of spatial and temporal trends in antibiotic consumption is important to understand the epidemiology of antibiotic resistance [113, 80]. The annual usage of antibiotics has been estimated to be between 100,000 and 200,000 tons globally, with more than 25 000 tons used each year in China [139]. Large volume of antibiotic drug consumption is a major driver of *antibiotic resistance* in the environment. Besides, growing up antibiotic resistance capacity among bacteria depends on the – volumes and patterns of antibiotic consumption [79, 89]. According to sales data of 71 countries, the consumption of standard units of antibiotics between 2000 and 2010 increased by (36%) wherein Brazil, Russia, India, China,

and South Africa accounted for (76%) of this increase [10, 41, 37, 23]. In most countries, antibiotic consumption varied significantly based on season. There was seen increased consumption of carbapenems (45%) and polymixins (13%), two last-resort classes of antibiotic drugs. The rise of antibiotic consumption and the increase in use of last-resort antibiotic drugs raises serious – public health concern [10, 42, 50]. Further, it is seen that large quantity of antibiotics are consumed in China, U.S., and India wherein major volume is used only in animal farms [32, 35].

Historical Origin of AR, ARBs and ARGs

Antibiotics have revolutionized medicine in many respects, and countless lives have been saved, their discovery was a turning point in human history. Regrettably, the use of these wonder drugs has been accompanied by the rapid appearance of resistant strains [68, 67]. Accidentally, antibiotic (Penicillin) was discovered by Alexander Fleming in 1929, and by the 1940s, penicillin was available for medical use and was successfully used to treat infections in soldiers during World War II [28, 24, 5]. In 1967 the first penicillin-resistant *Streptococcus pneumoniae* was observed in Australia, and seven years later, in the U.S. another case of penicillin-resistant *S. pneumoniae* was observed in a patient with pneumococcal meningitis [24, 31]. Antibiotic resistance by other organisms reflects the same trend observed between *S. pneumoniae* and penicillin. The increase in resistance among these organisms clearly indicates a change in the frequency of antibiotic resistance genes [112, 121]. However, microbes, their genes, interaction and horizontal transfer for creating resistance genes are shown in (figure 1).

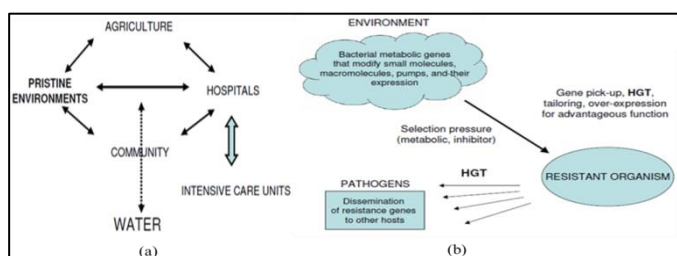


Fig. 1: (a) Microbes, their genes, populations and interactions, and (b) Role of horizontal gene transfer in the creation of resistance genes and their dissemination [26].

The chronological development of antibiotics and its resistance in the world is presented in (figure 2). Here, the dark ages – the preantibiotic era, primordial – the

advent of chemotherapy, golden – the halcyon years when most of the antibiotics used today were discovered, the lean years – the low point of new antibiotic discovery and development, pharmacologic – attempts were made to understand and improve the use of antibiotics by dosing and administration, biochemical – knowledge of the biochemical actions of antibiotics and resistance mechanisms led to chemical modification studies to avoid resistance, target – mode of action and genetic studies led to efforts to design new compounds, genomic/HTS – genome sequencing methodology was used to predict essential targets for incorporation into high-throughput screening assays, disenchantment – with the failure of the enormous investment in genome-based methods, many companies discontinued their discovery programs [112, 28, 4, 24]. Currently, numerous ARBs are spread in diverse environment, such as – water, wastewater, soil and animal manure. Consequently, the global initiatives to advance the sustainability of urban water infrastructure through adopting measures, for example – water reuse is facing problems because wastewater effluents are enriched in antibiotics, ARBs, and ARGs. Thus, water environment act as a source and pathway for the spread of antibiotic resistance [100, 15, 24]. Wherein, the dispersal of ‘foreign genes’ into the environment occur through – ‘horizontal gene transfer’ and ‘vertical gene flow’ by seed dispersal, pollen flow considered as major concern. There is substantial public concern about a potential spread of ARGs from transgenic plants into the soil and intestinal bacteria [26, 128]. On the other hand, the causes of antibiotic resistance are complex and include human behaviour at many levels of society [65]. However, the increasing levels of multi-drug resistance in human pathogenic bacteria are compromising our ability to treat infectious disease [116]. Besides, ARGs are biologically transmitted from microorganism to microorganism in particular micro-environments where dense microbial communities are often exposed to an intensive use of antibiotics [108, 100].

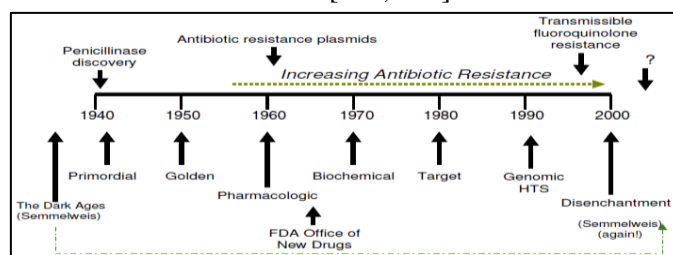


Fig. 2: The ages of antibiotic discovery and development of its resistance in the world [28].

Animal Farm and Wastewater: Heaven of ARGs

Antibiotics are produced by pharmaceutical industries while consumed by healthcare facilities (hospitals), veterinary, and animal farm (industry). Then, consumers discharge their daily generated wastes into water bodies or soil that are enriched – with antibiotics, ARBs and ARGs [97]. Indeed, the expansion of the ARG reservoir in the environment has been caused by antibiotic use in humans and animals [61]. Hence, many researchers have already detected animal farm and animal wastewater as *heaven* of ARGs [49, 127, 91]. The study by Van Boeckel et al. [126] is the first to estimate global use of antibiotics in livestock production, and to disaggregate that global figure into estimates for each of 228 countries and the scenario of antibiotic use in animal farm is shown in (figure 3). It was found that abattoir wastewater contained high levels of *Escherichia coli* and *Enterococcus spp.* wherein *Salmonella spp.* was not detected but *Citrobacter freundii* and *Shigella spp* in Uganda [119, 2, 135]. Currently, concerns about potential threats of antibiotics to humans and wildlife, has been highlighted. Antibiotics are commonly applied to animals to prevent diseases and promote growth making livestock agriculture a major source of – antibiotic pollution [102, 3]. So, the largest consumers of antibiotics in the world are human being and veterinary or animal farms. Therefore, intensive animal husbandry is believed to be a major contributor to the increased environmental burden of ARGs [148, 137, 117]. Through human and animal wastewater and excreta consumed antibiotics get mixed with surface water and sediment. By the way, both surface water and soil are becoming contaminated day-to-day [58, 70]. Despite of large volume of antibiotics are consumed in China, little information is available regarding the corresponding ARGs associated with animal farms. By using high-capacity qPCR arrays, 149 unique resistance genes are detected from – animal farms in China. Diverse, abundant, and potentially mobile ARGs in farm samples suggest that unmonitored use of antibiotics and metals is causing the emergence and release of ARGs to the environment [129,148, 11, 102]. Additionally, dairy lagoon water acts as reservoir of large quantity of ARGs that comes from animal farms. It was found that aerobic versus anaerobic treatment had no effect on tet(W), with an overall pattern of increase in the presence of antibiotics followed by decrease to initial levels. But tet(O) responded differently under aerobic versus

anaerobic treatment as well as sul(I) and sul (II) showed similar patterns [93, 39, 77]. The lowest concentrations of both tet and sul ARGs were found in the lagoons of chicken layer operation, in contrast, sul ARGs were detected highest in the – swine lagoons [77]. Anyhow, plasmids a mobilized agent carries ARGs from source to different environment. Incompatibility testing and PCR analysis clearly revealed at least two different types of IncQ-like plasmids. Both types of IncQ plasmids were detected in manure, sewage, and farm soil [115, 21]. In case of treatment, a chlorine dose close to breakpoint is required to achieve complete removal of antibiotics, leading to high consumption of free chlorine in most of the wastewaters [102, 93, 1].

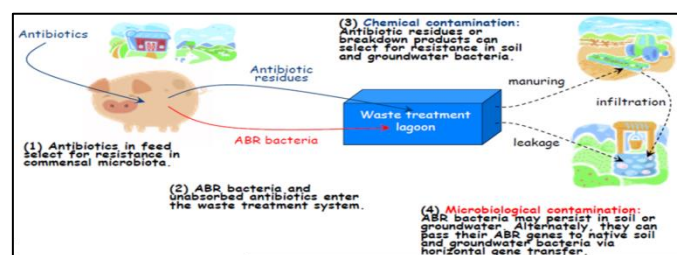


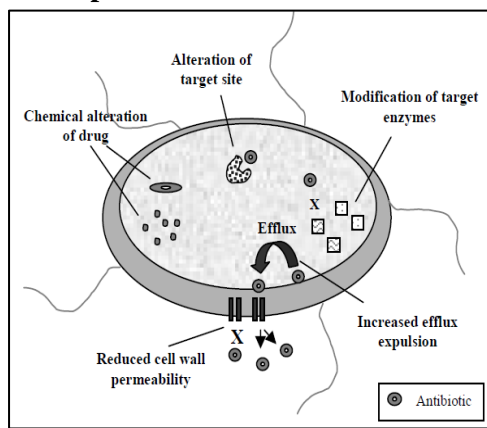
Fig. 3: Scenario of antibiotic use in animal production and its flow in environment [144].

Surface Water and Municipal Wastewater: Carriers of ARGs

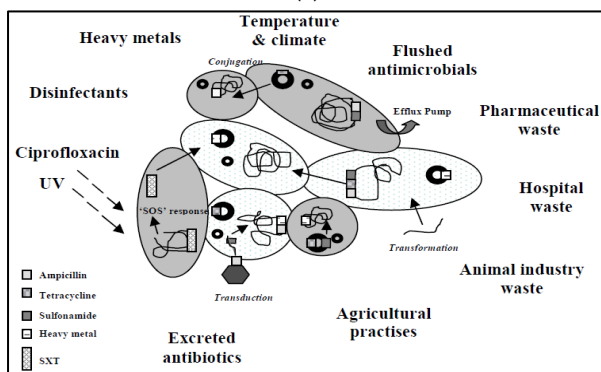
Since, life is fully dependent on water, so the protection of aquatic environments and water resources is crucial for – sustainability of human being. But water being universal solvent, it gets mixed with numerous impurities that makes water polluted; one of such pollutants is ARGs [102, 76]. The point sources of such ARGs are human being and animal, after consuming antibiotics, they release them into surface water and wastewater through excreta and feces [64, 131]. As example – five groups of antibiotics were investigated in the surface water of Yangtze Estuary over four seasons and detected 20 antibiotics without sulfamerazine. It was found that frequencies and concentrations of antibiotics depend on several factors, such as, flow conditions (seasonal), temperature and location (discharge and sewage outfall) [143, 150]. Similarly, it was found that high concentrations of antibiotics are related to urban and agricultural activities in Cache La Poudre River [92]. In Cache la Poudre (Poudre) and South Platte Rivers of Colorado, eight sites were classified as primarily WWTP-influenced based on discriminant analysis of ARG detection frequencies. By contrast, tet(W) phylotype and phylogenetics of site Poudre River-4,

located 4 km downstream of a WWTP, was also characterized and found to be significantly different from the animal feeding operation (AFO) lagoons. Generally, a good correspondence was found between classification of the impacted river sites and the surrounding landscape [118, 142, 140]. Further, the water environment may represent – a key dissemination pathway of resistance elements to and from humans. Riverine *sul1* is correlated with upstream capacities of animal feeding operations and wastewater treatment plants [99, 107]. Wherein tetracycline resistance genes were not detected by quantitative PCR in many samples but *sul1* and *sul2* were present at relatively high concentrations in all (38) samples collected from Haihe River, China. The highest ARG concentrations detected were in sediment samples collected during the summer, indicating that sediments are an important ARG reservoir than water in – Haihe River [72, 26]. Besides, hospital and municipal sewage are important sources of ARGs for the receiving freshwater bodies. Consequently, in freshwater lake sediments in the vicinity of a point source of treated wastewater wherein total and relative abundance of ARGs were identified in close proximity of the sewage discharge point and decreased exponentially with distance [25, 57].

Municipal WWTPs: Reservoir of ARGs



(a)



(b)

Fig. 4: (a) Schematic diagram depicting the major antimicrobial resistance mechanisms and (b) Illustration showing bacterial floc in STP, potential genetic events (*italics*) and influences (**bold**) leading to antibiotic resistance amongst environmental bacteria [55].

Wastewater treatment plants (WWTPs) serve a vital role for protection of human and environmental health and may represent a critical control point for the global spread of antibiotic resistance [64]. While the effluent of WWTPs is treated with a variety of antimicrobial methods, bacteria and the genetic material that is able to pass on antibiotic resistance to environmental populations (details figure 4) are not completely destroyed [74, 7]. Because, it receives direct input of antibiotics as well as resistant fecal and other commensal bacteria, while activated sludge can harbor bacteria resistant to clinically important antibiotics, including ciprofloxacin and vancomycin [84]. A unique aspect of ARGs as contaminants is that biological treatment steps may actually result in a selective increase of ARBs and ARGs [71, 77]. ARGs have been observed to persist in effluents of a variety of full-scale WWTPs at levels well above those typical of aquatic environments, even following mixed-media filtration and disinfection [60, 64]. It was found that mesophilic anaerobic digestion at both 10 and 20 day solids retention times (SRTs) significantly reduced *sul1*, *sulII*, *tet(C)*, *tet(G)*, and *tet(X)* with longer SRT exhibiting a greater extent of removal, however, *tet(W)*, *erm(B)* and *erm(F)* genes increased relative to the feed. Thermophilic anaerobic digesters performed similarly to each other and provided more effective reduction of *erm(B)*, *erm(F)*, *tet(O)*, and *tet(W)* compared to mesophilic digestion [73, 105]. Besides, water quality indicators and bacterial AR were examined at locations impacted by confined AFOs and compared them to nearby reference sites. Sites near confined AFO farms had poor water quality, while water quality remained relatively good downstream of WWTP. Out of a total of 830 environmental bacterial isolates, (77.1%) were resistant to only ampicillin, while (21.2%) were resistant to combinations of other antibiotics [132, 9].

MSW and Landfill Leachate: Breeding House of ARGs

Although antibiotic use in clinical settings is regulated, the disposal of antibiotics related to household use and PCPs is less discriminate, usually being disposed with other solid wastes [130, 100]. Thus, landfills are often receptacles of antibiotics and, in turn, possible incubators for the selection of resistant bacteria and

ARGs via HGT and other mechanisms due to long term exposures within – landfill ecosystems [122]. As such, waste antibiotics and resultant ARGs may pass from MSW into mobile leachates and then into surrounding environments [43, 122], although relative leachate levels and relationships over space and time across MSW networks have not been assessed in great detail [52, 33]. Emerging contaminants (ECs) are compounds that recently have been shown to occur widely in the environment and identified as being a potential environmental or public health risk, but yet adequate data do not exist to determine their risk. However, ECs viz. pharmaceuticals, PCPs, surfactants, plasticizers, fire retardants, pesticides and nanomaterials's source, fate and transport in landfill leachate and adjacent environments [103]. Lately, 20 antibiotics and six ARGs were detected in MSW leachates from two Shanghai transfer stations (TS) and one landfill reservoir (LR) in April and July 2014. Antibiotic levels were higher in TS than LR leachates. However, ARG abundances did not correlate with detected antibiotic levels, except for tetW and tetQ with TC levels. In contrast, most measured ARGs did significantly correlate with heavy metal levels ($p < 0.05$), especially with Cd and Cr [138, 22, 29].

Soil and Animal Manure: Potential Harbour of ARGs

Several studies have examined the effect of manure application on antibiotic resistance in soil from various perspectives [110, 13]. Effects of swine manure application on sul1, sul2, ermF, ermB, tet(Q), and tet(X) abundance have been studied in detail in soil, while newer metagenomic approaches have revealed increases in a variety of ARGs [49, 54, 149]. Increases in ARG abundance in soil have been associated with manure spiked with antibiotics; livestock fed antibiotics compared to those not fed antibiotics, the presence of metals [53, 62]. However, manure application does not universally increase ARGs in soils [38, 141, 47]. Cultured microorganisms have been commonly focused in attempts to isolate ARGs or to identify antimicrobial compounds. Although this strategy has been successful in many cases, most of the microbial diversity and related antimicrobial molecules have been completely lost [16]. Before and after application of dairy manure slurry and a dry stack mixture of equine, bovine, and ovine manure showed that growth of bacterial hosts containing ARGs or horizontal gene transfer immediately following slurry application with respect to

ermF, sul1, and sul2 and following a lag for dry-stack-amended soils [36, 19]. Besides, soil bacteria are a reservoir of ARGs with greater genetic diversity than previously accounted for, and that the diversity can be surveyed by a culture-independent method [104]. The fate of added microorganisms can also be related to the fate of their DNA or any DNA found within soil or groundwater. The genes were located on a plasmid pLEP01, which was either introduced into the soil columns directly as a mixture of supercoiled and open circular forms or after linearization by restriction enzymes [96, 109, 40]. Both cattle slurry (CS) and CS digestate are a considerable ARG, especially sulphonamide resistance encoding sul1. Mineral or organic fertilizers amendment significantly affects ARG concentration and proportion in bacterial community in grass land soil. While, ARG concentration levels are significantly different corresponding to different fertilization treatments [86, 63]. It is estimated that approximately (75%) of antibiotics are not absorbed by animals and are excreted in waste. Antibiotic resistance selection occurs among gastrointestinal bacteria, which are also excreted in manure and stored in waste holding systems [19]. Veterinary antibiotics used in animal husbandry are assumed to contribute to an increased antibiotic resistance amongst bacteria in manure. Bacteria carrying transferable ARs, antibiotics, metabolites and nutrients are inevitably brought into soil when manure is used as fertilizer [48, 88, 54].

Organic Agriculture Increase Antibiotic Resistance in Soil

Microbial resistance to antibiotics is on the rise, in part because of inappropriate use of antibiotics in human medicine but also because of practices in the agricultural industry. The resistant bacteria from agricultural environments may be transmitted to humans (shown in figure 5), in whom they cause disease that cannot be treated by conventional antibiotics [56, 148]. If genes for antibiotic resistance are linked to genes for the desirable trait, researchers can single out plant cells that have been transformed successfully by exposing all cells to an antibiotic. This means, however, that some new varieties of plants with desirable traits, such as insect resistance or herbicide tolerance, may also carry a new gene for antibiotic resistance [20, 46, 137]. Both animals and humans may excrete up to (95%) of antibiotics in an unaltered state. While, some antibiotic removal has been observed in WWTPs and in agricultural waste treatment

systems, none of the systems are designed to remove antibiotics [45, 59]. ARG diversity, abundance and antibiotic molecule exposure are, however, not systematically linked, and many other factors can contribute to resistance gene emergence, selection and dissemination in the environment. Soil is a heterogeneous habitat and represents a broad spectrum of different ecological niches [85, 95]. The use of antibiotics in agriculture is routinely described as a major contributor to the clinical problem of resistant disease in human medicine. While a link is plausible, there are no data conclusively showing the magnitude of the threat emerging from agriculture [18, 8, 53]. Environmental bacteria which contain ARGs identical to those in enteric bacteria have acquired the genes by 'horizontal transfer'. On-farm the fate and impacts of estrogenic hormones in field soils receiving swine manure is being evaluated on 3 farms in SW Ontario wherein the persistence, pathways, and rate-controlling parameters of estradiol breakdown are being determined in agricultural soils [123, 146]. Streptomycin is used in several countries, the use of oxytetracycline, oxolinic acid and gentamicin is limited to only a few countries. Antibiotics are applied when disease risk is high. However, antibiotics have been indispensable for crop protection in the U.S. for more than 50 years without any reports of adverse effects on health or persistent impacts on the environment [117, 49].

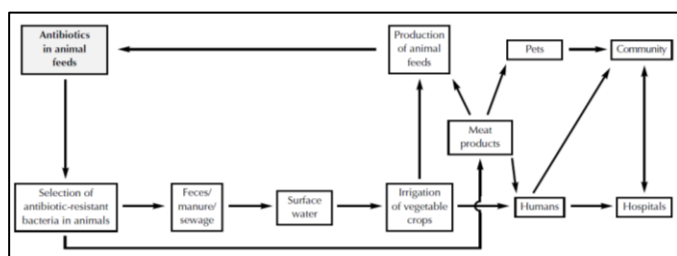


Fig. 5: The agricultural use of antibiotics in animal feed can result in the selection and transmission of antibiotic-resistant bacteria. These bacteria move through the environment by a variety of routes, and their presence ultimately has consequences for human health [56].

Treatment and Disinfection of ARGs in Wastewater

Disinfection of wastewater may present an opportunity to limit release of ARGs to the environment and ultimately reduce the risk of spreading to pathogens and contributing to drug resistant infections in humans (details in figure 6) [78, 12]. UV disinfection is of particular interest because UV radiation is directly absorbed by DNA and thus has the potential to impart

ARG damage [125, 30]. UV disinfection is commonly employed for seasonal disinfection, is thought to be limited in production of disinfection byproducts, is relatively noncorrosive to water treatment and delivery systems, and does not leave a residue, which could be damaging to receiving environments [7, 60, 81]. In a study, free chlorine was applied to oxidize antibiotics and to disinfect lagoon bacteria as well. Results indicate that aeration substantially improves lagoon functionality, thereby adding both organic and ammonia removal. Ammonia present in the wastewaters plays a critical role in antibiotics decomposition and bacterial inactivation due to its rapid competition for free chlorine to form monochloramine. Generally, a chlorine dose close to breakpoint is required to achieve complete removal of antibiotics [102, 145]. However, UV disinfection technology as the potential way to damage four ARGs, *mec(A)*, *van(A)*, *tet(A)*, and *amp(C)*, both in extracellular form and present within a host ARBs: methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin resistant *Enterococcus faecium* (VRE), *Escherichia coli* SMS-3-5, and *Pseudomonas aeruginosa* 01, respectively. In general, damage of ARGs required much greater UV doses than ARB inactivation. Overall, the results indicate that UV is limited in its potential to damage ARGs [78, 51]. Among chlorination, ultraviolet (UV) irradiation and sequential UV/chlorination treatment on the inactivation of ARGs, a positive correlation was observed between the removal of ARGs and chlorine dosage, as well as contact time. Greater free chlorine (FC) dosage leads to higher removal for all the genes. Wherein, NH₃-N concentration was found to lead to lower removal of ARGs at the same chlorine dosage [147, 114, 83]. Significant removal of ARGs was achieved by membranes of 100 kDa and smaller, and presence of wastewater colloids resulted in enhanced removal by 10 kDa and 1 kDa membranes. ARG removal was observed to correlate significantly with the corresponding protein, polysaccharide, and total organic carbon colloidal fractions. Therefore, advanced membrane treatment technology is promising for managing public health risks of ARGs in wastewater effluents [12, 14]. There is widespread speculation that WWTPs and aquatic environments in general maybe a breeding ground for ARBs. The presence of antibiotics in WWTPs facilitates the acquisition and proliferation of resistance characteristics amongst bacteria in that environment [55, 120, 82].

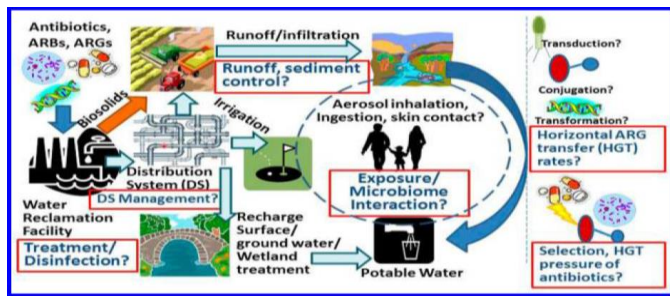


Fig. 6: Potential for water and nutrient reclamation approaches to contribute to the spread of antibiotic resistance. Red boxes indicate key research questions that should be addressed to advance risk assessment and risk management. DS = distribution system [100].

III. CONCLUSION

Modern world can't be thought a single day without use of – antibiotics for human being and animal. But the ever growing unmonitored and uncontrolled consumption of antibiotics as well as heavy metals is responsible for growing resistance capacity among different bacteria, ultimate result of which is spread of ARBs and ARGs in environment. A large volume of antibiotics is used only in animal farms of China, U.S., India, Russia and Brazil. Thus, human and animal consumed antibiotics and ARs are dispersing into different environment through – wastewater, animal manure, organic fertilizer, soil, and solid wastes. However, in China swine farms are considered as hotspots of ARGs. But mass people are not aware about such silent emerging contamination worldwide, therefore, it is creating global problems for environment and public health. However, the causes of ARGs spread are detected but still it is no well-established technique to inactivate or remove ARGs from such reservoirs. In contrast, it is found that conventional wastewater treatment technologies aren't sufficient to remove ARGs from water but – high dose of free chlorine, UV ozonation and advanced membrane treatment technologies can remove more ARGs from wastewater.

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