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A review of the influence of treatment strategies on antibiotic resistant bacteria and antibiotic resistance genes

Virender K. Sharma [a,*], Natalie Johnson [a], Leslie Cizmas [a], Thomas J. McDonald [a], Hyunook Kim [b]

[a] Department of Environmental and Occupational Health, School of Public Health, Texas A&M University, College Station, TX 77843, USA
[b] Department of Energy & Environmental System Engineering, The University of Seoul, 90 Jeonnong-dong Dongdaemun-gu, Seoul 130-743, Republic of Korea

HIGHLIGHTS

- Prevalence of ARB and ARG in rivers, lakes, surface water, wastewater, and sludge.
- Mechanism of resistance include horizontal gene transfer from donor bacteria.
- Chlorine and advanced oxidation processes inactivate ARB and ARG significantly.
- Flow pattern of the constructed wetlands governs removal of ARB and ARG.
- Nanoparticles have a role in investigating mechanism of transfer of ARG from genera.

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ABSTRACT

Antibiotic resistant bacteria (ARB) and antibiotic resistance genes (ARG) in the aquatic environment have become an emerging contaminant issue, which has implications for human and ecological health. This review begins with an introduction to the occurrence of ARB and ARG in different environmental systems such as natural environments and drinking water resources. For example, ARG or ARB with resistance to ciprofloxacin, sulfamethoxazole, trimethoprim, quinolone, vancomycin, or tetracycline (e.g., *tet*(A), *tet*(B), *tet*(C), *tet*(G), *tet*(O), *tet*(M), *tet*(W), *sul* I, and *sul* II) have been detected in the environment. The development of resistance may be intrinsic, may be acquired through spontaneous mutations (*de novo*), or may occur due to horizontal gene transfer from donor bacteria, phages, or free DNA to recipient bacteria. An overview is also provided of the current knowledge regarding inactivation of ARB and ARG, and the mechanism of the effects of different disinfection processes in water and wastewater (chlorination, UV irradiation, Fenton reaction, ozonation, and photocatalytic oxidation). The effects of constructed wetlands and nanotechnology on ARB and ARG are also summarized.

1. Introduction

Access to safe and clean water is a prerequisite for meeting the standards of living in the modern society, but more than one billion people lack access to safe drinking water (Shannon et al., 2008). In the 20th century, safe potable water was achieved through filtration and chlorination; however the water infrastructure of the 21st century is not adequate to meet the challenges of water contamination (Pruden, 2014). For example, many regions of the world such as the Middle East and highly populated urban areas (e.g., Singapore) are struggling to attain water sustainability. Water infrastructure continues to encounter threats from a rising number of contaminants while the treatment systems are not able to effectively treat emerging pollutants. The presence of contaminants in water resources negatively affects public and environmental health (Hong et al., 2015; Richardson and Ternes, 2014).

Generally, unregulated pollutants are referred to as emerging contaminants which include gasoline additives, surfactants, endocrine disruptors, and pharmaceuticals and personal care products (PPCP) (Picó and Barceló, 2015). In recent years, the focus has been on pharmaceuticals as important emerging contaminants, which

* Corresponding author.
E-mail address: vsharma@sph.tamhsc.edu (V.K. Sharma).

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are of concern due to their increasing use worldwide (Khetan and Collins, 2007). A number of pharmaceuticals are not fully removed by wastewater treatment, and effluents are discharged directly into water bodies. Consequently, pharmaceuticals are frequently found in the aquatic environment (Banjac et al., 2015; Evgenidou et al., 2015; Kim et al., 2013; Luo et al., 2014; Verlicchi et al., 2015). Examples of detection of pharmaceuticals in drinking water, ground water, and wastewater include iodinated X-ray contrast media (ICM) in Germany, antidepressants in the United States, and Canada, antibiotics in Australia, and numerous other drugs molecules in the European Union, China, and the United States (Michael et al., 2013; Postigo and Richardson, 2014; Tölgyesi et al., 2010). The persistence of these molecules in different water bodies may pose a risk to aquatic life (Cizmas et al., 2015; de Jesus Gaffney et al., 2015; Li et al., 2015b).

Among the pharmaceuticals, antibiotics have received great attention. Antibiotics are mainly applied to treat bacterial infections, which are a major public health issue. In the United States alone, infections caused at least 2 million serious illnesses and contributed to about 23,000 deaths each year (Friedman, 2015; Rosi-Marshall and Kelly, 2015). Antibiotics are classified into different categories such as sulfonamides, antibiotics, macrolides, β-lactams, pencillins, arsenicals, and aminoglycosides (Bouki et al., 2013; Fatta-Kassinos et al., 2011; Jiang et al., 2013). In the United States, over 250 million antibiotic prescriptions are written annually (Rosi-Marshall and Kelly, 2015). In agriculture, antibiotics are used as veterinary medicine, as biocides in the production of fruit and crops, and as feed additives for livestock and poultry (Table 1) (Silbergeld et al., 2008). The antibiotics shown in Table 1 represent most of the major classes of antimicrobials. Third generation cephalosporin molecules are also included in Table 1. In China, 46% of the 210,000 tons of antibiotics produced annually are being used for animal husbandry (Su et al., 2014). The intensive application of antibiotics in agriculture worldwide has resulted in the release of large amounts of antibiotics to the environment (Silbergeld et al., 2008).

Antibiotics enter into the environment through animal manure and human wastes, which contain significant concentrations of non-metabolized antimicrobials (Berendonk et al., 2015; Martinez, 2008). The fate of antibiotics is determined by their biological and physico-chemical properties (Kim et al., 2014; Kümmerer, 2009a, 2009b; Oncu and Balcioglu, 2013; Sharma et al., 2013). Antibiotics can be persistent in the environment and therefore have been detected in water resources (Gothwal and Shashidhar, 2015; Luo et al., 2014; Verlicchi et al., 2015). There is growing concern that unused antibiotics in the surface water may be causing a risk to human health by promoting antibiotic resistant bacteria (ARB) and antibiotic resistance genes (ARG) (Berendonk et al., 2015). Furthermore, antibiotics in ecosystems can influence the evolution of microbial structure and thus may pose a risk to ecological health (Berendonk et al., 2015; Bouki et al., 2013; Martinez, 2008; Rosi-Marshall and Kelly, 2015).

According to the World Health Organization, antibiotic resistance has become a critical global public health issue of this century. ARB have been found in different aquatic environments (Leonard et al., 2015). Examples of ARB that are usually of concern in healthcare practices are the enterococci, *Klebsiella pneumonia* and *Pseudomonas* spp (Bouki et al., 2013). ARG have also emerged as environmental contaminants (Hsu et al., 2015). ARG have a capacity to spread among bacteria and distribute from human and animal sources to natural environments and drinking water resources (Berendonk et al., 2015; Gillings et al., 2015; Martinez, 2008; Storteboom et al., 2010). ARG have been found in a wide range of environmental matrices, including sediments, lakes, rivers, soils, and wastewater treatment plant effluents. Sediment samples, collected from the Netherlands, showed an increasing trend in ARG during 1940–2008, which conferred resistance to macrolides, penicillins, and tetracyclines (Knapp et al., 2010). ARG were also observed in the sediments and water of Lake Geneva (Czekalski et al., 2015; Thevenon et al., 2012). In the investigation of ARG in the Yangtze River Delta, China, ten tetracycline and sulfonamide resistance genes (*tet*(A), *tet*(B), *tet*(C), *tet*(G), *tet*(O), *tet*(M), *tet*(W), *sul* I, and *sul* II) were detected (Guo et al., 2014). ARG or ARB with resistance to ciprofloxacin, sulfamethoxazole, trimethoprim, quinolone, vancomycin, or tetracycline have been detected in effluents of urban residential areas, hospitals, and a municipal wastewater

Table 1
Antimicrobials that have been registered for use as feed additives in the United States, Canada, European Union, and Australia (adapted from (Silbergeld et al., 2008) with permission from Annual Reviews.).

Group/Class	Antimicrobial	Usage
Arsenicals	3-nitro-arsenic acid	Pigs, Poultry
	Arsenilic acid	Poultry
	Roxarsone, Cabarsone	Poultry
Glycopeptides	Avoparcin	Pigs, Poultry, Cattle
Polypeptides	Bacitracin	Meat poultry, Labs, Pigs, Calves, andTurkeys
Polyethers (Ionophores)	Lasalocid	Cattle
	Narasin	Cattle
	Salinomycin	Pigs, Cattle
	Monensin	Cattle (growth promoters)
Macrolides	Kitasamycin	Pigs
	Oleandomycin	Cattle
	Tylosin	Pigs, Cattle, and Chicken
	Spiramycin	Turkeys, Chickens, Calves, Pigs, and Lambs
	Erythomycin	Chickens
	Tiamulin	Pigs
Quinoxalines	Olaquindox	Pigs
	Carbadox	Pigs
Streptogramins	Virginiamycin	Pigs, Cattle, Poultry, Turkey, Laying hens, Calves, Swine, and Sows
Penicillins	Pencillin G	Chicken
	Pencillin G procaine	Chicken, Turkey, and Sleep
Tetracyclines	Chlorotetracycline	Chicken
	Oxytetracycline	Turkey, Cattle, Sheep, and Swine
Sulfonamides	Tetracycline	Pigs
	Sulfamethazine	Pigs, Cattle
	Sulfathiazole	Pigs