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### Antimicrobial resistance: the role of aquatic environments

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#### A B S T R A C T

Antimicrobial resistance is a major concern worldwide. Antibiotics are one of the most used drugs in humans and animals. The intensive use of antimicrobial agents is one of the main factors for the generation of resistant bacteria. Infections with resistant organisms and the emergence of multi-drug resistant pathogenic and non-pathogenic bacteria, represents an urgent global challenge since increases the incidence of morbidity and mortality and decreases the effectiveness of infectious diseases treatments. Many of the encoding antimicrobial resistant genes from human pathogens have originated in natural environments. Anthropogenic activities on aquatic environments, sediments and soils, such as hospital, pharmaceuticals and municipals discharges into rivers and lakes increase the generation of new resistance genes and the spread of resistant bacteria in the environment as well as in public health. This highlights the importance of the environment as a reservoir of resistance genes and dispersal vector. It is necessary to take measures to reduce the introduction and spread of resistant bacteria and its determinants in the environment, which could contain diverse chemicals, antibiotic residues or quaternary ammonium compounds. These measures include the management of wastewater treatment.

#### Introduction

An antibiotic is a chemotherapeutic agent that inhibits or abolishes the growth of

microorganisms, such as bacteria, fungi, or protozoa (Kümmerer, 2009a). They could be

natural (produced by micro-organisms), semi-synthetics (derivatives of natural antibiotics with structural modifications) and fully synthetics. Several antibiotics are produced by environmental microorganisms, including bacteria within soils and water (Finley et al., 2013). Thus, genes for antibiotic resistance must also have emerged in non-clinical habitats (Martínez, 2008). Antibiotics are widely used for prevent infections in human being and animals, as growth promoters in animal's husbandry and as prophylactic treatment in aquaculture. Thus, it is a priority conserves the antibiotic efficacy. Nevertheless, resistance to all classes of antibiotics has emerged, and there are no antibiotics for which resistance does not exist (Wright, 2010). For decades, clinicians and scientist have asked to make rational use of antibiotics, in an effort to avoid antibiotic resistance and its dispersion in the environment. However, the intensive use, misuse and the selection pressure applied by antibiotics used in clinical and agricultural settings have promoted the evolution and spread of genes that confer resistance (Allen et al., 2010).

After the administration, antibiotics are excreted unchanged and/or not fully metabolized into the environment (Kümmerer, 2003). Therefore, a mixture of pharmaceuticals and their metabolites will enter municipal sewage and wastewater treatment plants (WWTP) (Kümmerer, 2004), and can reach the environment. In recent years, antibiotics contamination is recognized as an emerging environmental pollution in aquatic environments, because of their potential adverse effects on the ecosystem and human health (Huang et al., 2001; Kümmerer, 2009a). The anthropogenic activities (including sewage discharge, wastewater treatment, drug manufacturing and intensive agricultural livestock) are changing environmental

reservoirs of resistance genes and their precursors: "*the resistome*" (D'Costa et al., 2006; Finley et al., 2013). Thus, the probability of recruitment of resistance genes into clinically relevant pathogens will increase (Peak et al., 2007; Knapp et al. 2011; Finley et al., 2013) because environmental bacteria act as an unlimited source of genes that might be resistance genes when entering in pathogenic organisms (Baquero et al., 2008). Furthermore, as pharmaceuticals are constantly released into the environment, organisms will be exposed to many of these compounds for their entire lifetime, exerting their effect on endogenous environmental bacteria (Boxall, 2004). Therefore, it is a concern, the potential bioaccumulation and persistence of released pharmaceuticals (Hernandes-Coutinho et al., 2013). It is highly importance to consider the environment when is intended the management of the antibiotic resistance and their spread into public health. A better understanding of antibiotic resistance prevalence and diversity in the environment will help elucidate resistant gene movement between environmental and clinical pathogenic bacteria (Martínez, 2008). In this review, is discussed how antimicrobial resistance and their determinants arise and disseminate in natural environments, focusing in aquatic environments and the anthropogenic impact on them.

### **The resistome: link between clinic and environment**

Antibiotics and resistance mechanisms are ancient. Environmental bacteria harboring resistance mechanisms against  $\beta$ -lactams, vancomycin and tetracycline may be more than 30,000 years old (D'Costa et al., 2011). Indeed, some natural antibiotic resistance bacteria appeared on the planet over 100 million years ago (Hernandes-Coutinho et al., 2010). The antibiotic "*resistome*" is the

collection of all genes that directly or indirectly contribute to antibiotic resistance, in both, the environment and the clinic background (Perry et al., 2013). The “resistome” includes the genes that codify for the resistance determines as well as their precursors that could be linked to antimicrobial resistance (Figure 1) (Wright, 2007). The environmental “resistome” is a significant source of resistance genes, and it has been theorized that antibiotic producing organisms in the environment are the source of resistance genes found in clinical pathogens (Perry et al., 2013). Therefore, environmental bacteria carry genes encoding resistance to antibiotics have become critically important in public health (D’Costa et al., 2011).

One of the more distinctive characteristics of microbial genomics is the movement of genes vertically (through populations by cell division), and horizontally (across species and genera) (Perry et al., 2013). This movement is allowed by the “*mobilome*,” the genetic elements that facilitate and contribute to horizontal gene transfer (HGT) (Siefert, 2009; Gaze et al., 2013). Three principal mechanisms are involved in HGT: conjugation (direct cell-to-cell transfer), transduction (phage-assisted transfer), and natural transformation (DNA-to-cell transfer, Figure 1). These mechanisms mobilize genetic elements, such as plasmids, genetic islands, and phages that can contain resistance elements (Colomer-Lluch et al., 2011; Heuer et al., 2012; Gaze et al., 2013). Furthermore, resistance gene cassettes can be collected by integrons that drive tandem genes from a single promoter element offering stunning multidrug resistance phenotypes (Patridge et al., 2009). Moreover, resistance genes can be mobilized within the chromosome and to plasmids by transposable elements (Gaze et al., 2013). The “*mobilome*” is key to the spread of genes encoding resistance to antimicrobial

drugs and heavy metals, and for pathogenic traits among bacteria which is helped by the movement through the environment (Hawkey et al., 2009). Thus, no regions are safe or can escape the introduction and movement of antimicrobial drug-resistant organisms and their genes (Gaze et al., 2013). Moreover, this mobilization is enhanced by the selection pressure applied by human activities, providing the opportunity of natural bacteria and bacteria introduced by anthropogenic way into the environment for multiple-resistant phenotypes (Gaze et al., 2013).

One example of antimicrobial resistance exchange between clinical and environmental resistomes is shown in the class-A extended-spectrum  $\beta$ -lactamase CTX-M, found on plasmids carried by the globally important pathogens and traced to environmental *Kluyvera* spp. (Humeniuk et al., 2000), and the quinolone resistance gene *qnr*, found on a broad-host range conjugative plasmid from a ciprofloxacin-resistant strain of *Klebsiella pneumoniae* and traced to the environmental water-borne species *Vibrio*, *Shewanella*, and *Aeromonas* (Poirel et al., 2005; Baquero et al., 2008; Cattoir et al., 2008). Forsberg et al. (2012) also showed evidence of resistance exchange from the two backgrounds. They showed a multi-drug resistant in Proteobacteria isolated from soil, which contain resistance cassettes against five classes of antibiotics ( $\beta$ -lactams, aminoglycosides, amphenicols, sulfonamides, and tetracyclines) that have perfect nucleotide match to genes from diverse human pathogen. Thus, the environmental resistome represents a deep pool reservoir of antimicrobial drug resistance elements that can be readily mobilized into human pathogens resulting in disease that is increasingly challenging to treat (Gaze et al., 2013).

Figure.1 Microbial resistome: resistance mechanisms and spread of drug resistance

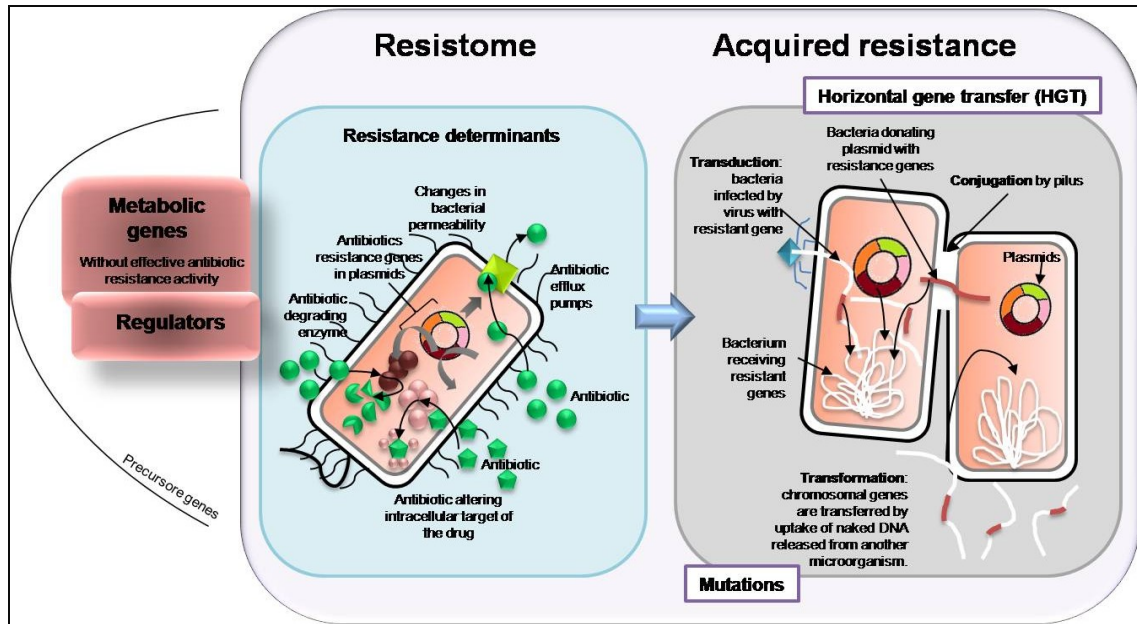
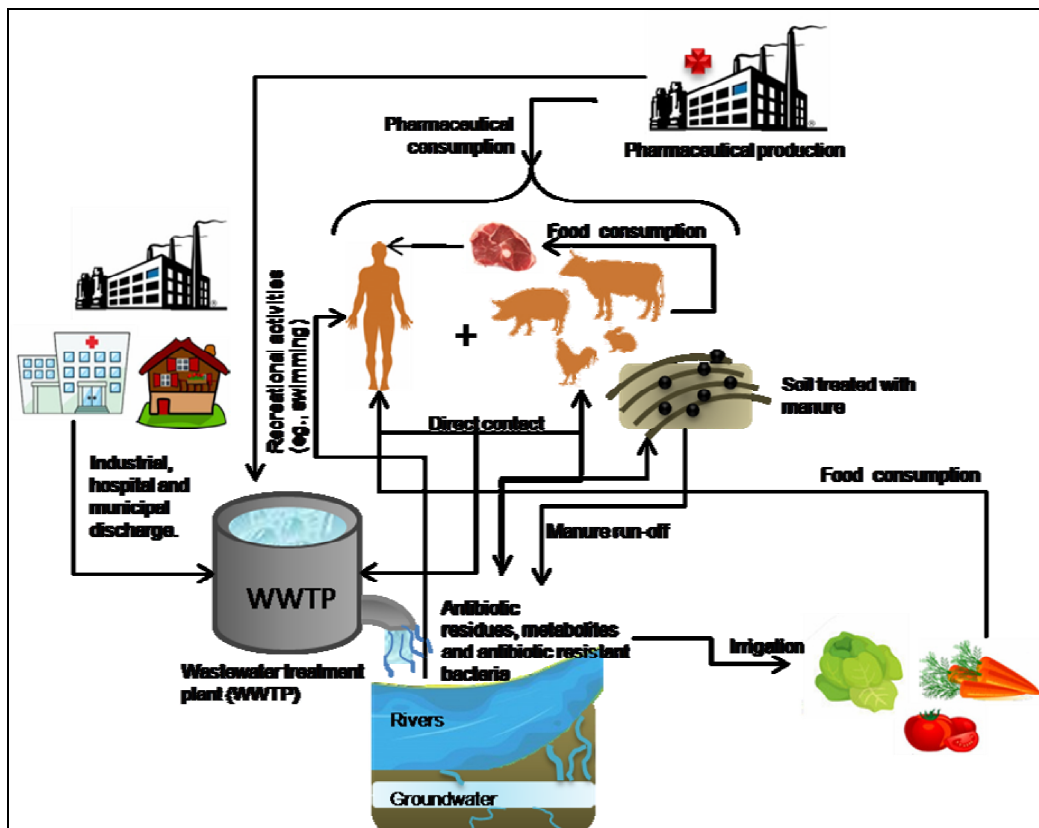
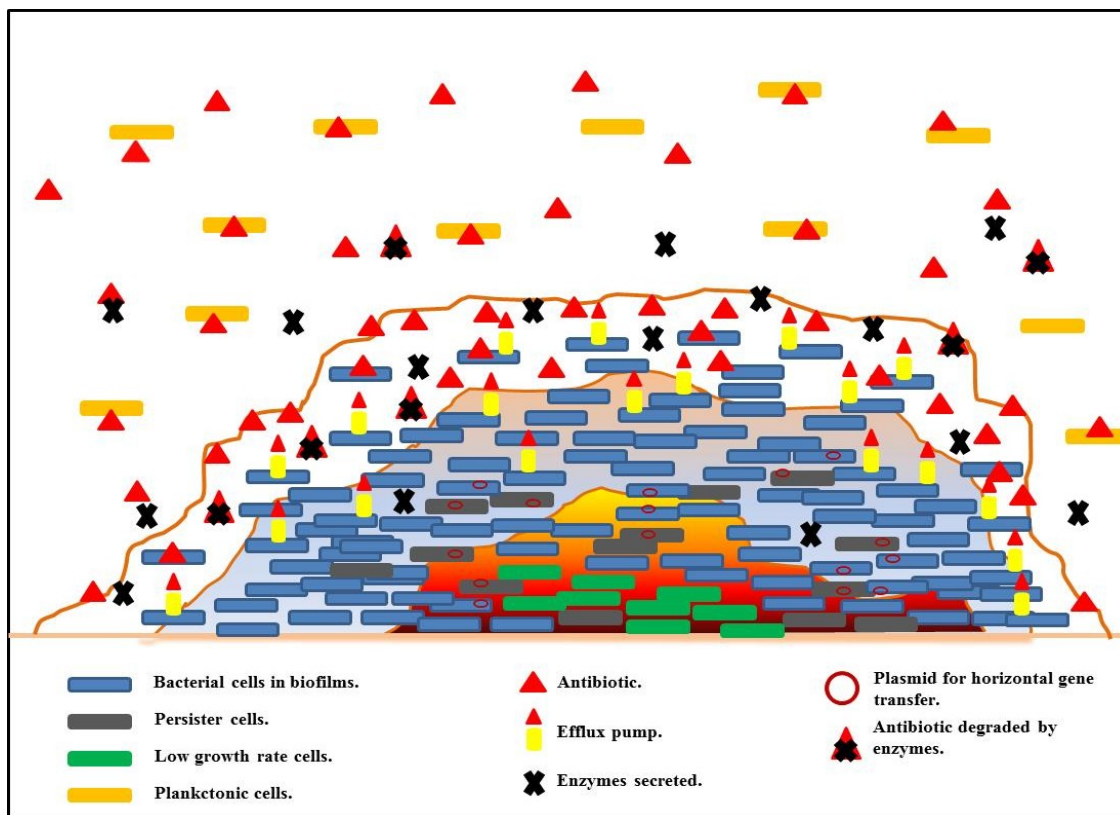


Figure.2 Presence and fate of pharmaceuticals in the environment



**Figure.3** Antimicrobial resistance in biofilms. Resistance to antimicrobial agents is the most important cause of non effective therapy of biofilm-associated infections. The increased resistance of bacteria is due to: 1) Difficulty of diffusion of antibiotics in to them and electrostatic charge of the exopolysaccharides which attract oppositely charged antibiotics. 2) A low growth rate. 3) Changes in phenotype acquired by bacteria forming biofilms. 4) Inactivation of antibiotics by polymers and enzymes secreted by bacteria



### Antibiotics spread in aquatic environments

One of the main routes of spread of pathogenic and/or antibiotic resistant bacteria is the environment, including water, soil and air. Multi-drug resistant bacteria have been detected in various water sources including rivers, lakes, groundwater and drinking water (Hamelin et al., 2006; Hamelin et al., 2007; Lindberg et al., 2007; Managaki et al., 2007; Thomas et al., 2007; Baquero et al., 2008; Gulkowska et al., 2008; Marti et al., 2013; Ramírez-Castillo et al., 2013). Consumption and handling of water, whether treated or untreated, can lead

to colonization of the gastrointestinal tract of humans and animals by bacteria containing resistance genes and exchange genes with bacteria already present in the intestinal tract (Baquero et al., 2008; Coleman et al., 2012; Finley et al., 2013). After use the antimicrobial agents, antibiotics and metabolites can directly enter to the environment through discharges from antimicrobial industries producing (Fick et al., 2009; Wellington et al., 2013), slurry, manure run-off, municipal and hospital discharges and sewage system (Figure 2).

Industrial and municipal discharges containing antibiotics generally at low concentrations, reach WWTP, and by contact with activated sludge encountered during the processing of wastewater, it may associated with these and enter into agriculture land when sludge are used as fertilizers (Kinney et al., 2006). Furthermore, irrigation with treated water and surface water is also a way for antibiotics entering agricultural soils (Kinney et al., 2006), then, contaminating products of human consumption with antibiotics (Finley et al., 2013). Veterinary pharmaceuticals and their metabolites can be released directly into the environment due to the use in aquaculture and treatment of farming animals, or indirectly during application of manure and slurry from intensive livestock (Boxall et al., 2004). Moreover, compounds that are released onto the soil and can be transported by surface water and groundwater (Blackwell et al., 2007; Topp et al., 2008) and even can be cycled and re-cycled in the environment (Wellington et al., 2013).

Indeed, more than 100 antibiotics have been detected in rivers, lakes and streams throughout the world at concentrations from nanogram(ng) until ug/L (Daughton and Ternes, 1999; Jorgensen and Halling-Sorensen, 2000; Kümmerer, 2001). In surface water, antibiotics are often detected, except for the pristine sites in mountains before streams reach urban and agricultural areas (Yang and Carlson, 2003). Nevertheless, some antibiotics had been found in groundwater even as deep as more than 10 m (Batt et al., 2006).

Humans and animals can be exposed to antibiotics, antimicrobial resistance genes or resistant bacteria in the environment by different pathways (Figure 2): cultures exposed to activated and/or sludge, animals (chicken, cattle, pig, etc.) that have been

treated with antibiotics as drugs or growth promoters, groundwater and surface water containing residues of pharmaceuticals and used as drinking water or irrigation, inhalation of dust emitted by livestock facilities and food crops (Heberer et al., 2002; Hamscher et al., 2003; Kumar et al., 2005; Boxall et al., 2006; Farkas et al., 2007, Benotti et al., 2009; Wellington et al., 2013).

Fresh water also serves as an important vehicle for spreading antibiotic resistance (Lupo et al., 2012). In fact, the newly recent New Delhi metallo- $\beta$ -lactamas (NDM-1) gene, which confers resistance to  $\beta$ -lactams, was found in high prevalence in chlorinated drinking water in India (Baquero et al., 2008; Walsh et al., 2011).

Although antibiotics may persist in the environment for long periods (months or years, e.g., tetracyclines and fluoroquinolones) and some of them may not be biodegradable (Kay et al., 2004; Boxall et al., 2006; Monteiro et al., 2010), these pollutants are not reported as toxic, persistent or bioaccumulative substances. Thus, few efforts have been made to avoid contamination by pharmaceuticals in the environment even though its prevalence is noticeable (Kümmerer, 2009; Wellington et al., 2013).

An example of the effect of antibiotic contamination is that of the quinolone resistance gene *qnr*, which is present in the chromosomes of waterborne bacteria (Poirel et al., 2005), after being integrated in plasmid, where it is constitutively expressed, *qnr* contributes to low-level of resistance to fluoroquinolones (Martinez-Martinez et al., 1998). Furthermore, other types of contaminations such as heavy metal pollutions (McArthur and Tuck field, 2000), quaternary ammonium compounds (QAC)

(Hegstadet et al., 2010) and personal care products might result in the presence of antimicrobial resistant bacteria. Stress conditions, which are usually found in polluted environments, have also the potential to increase recombination and HGT favoring the dissemination of antibiotic resistance genes (Beaber et al., 2004; Martínez, 2008). It is notice that, anthropogenic activities increase in the concentration of antibiotics in natural ecosystems influence antibiotic resistance, and may also affect the diversity of microbial population dynamics in different natural environments (Martinez, 2008).

### **The impact of the wastewater treatment plants in the antibiotic resistance**

The importance of water environments for gene exchange is that they are mixing environmental and clinical organisms, including pathogenic bacteria (Perry et al., 2013). Antibiotics and antibiotic resistant bacteria (ARB) can enter into WWTP through various sources, such as industrial waste, hospital discharges and municipal discharges and run-off manure from intensive livestock. Both, antibiotics and ARB, are affected by the different treatment process. Untreated wastewater in the WWTP are important reservoirs for human and animals commensal and pathogenic bacteria in which antibiotic resistant organisms persist and as well as their determinants (Zhang et al., 2009). Furthermore, since microbial density is usually high, and is conform from diversity on microorganisms (commensal bacteria, environmental microorganisms, clinically pathogens, and biofilms from activated sludge), may facilitate the antibiotic resistant dissemination by HGT (Schluter et al., 2007; LaPara et al., 2012).

Usually, the WWTPs reduce concentrations of nutrients in the water and thus, the total

number of bacteria at the end of the treatment (Zhang et al., 2007). However, even resistant bacteria are eliminated quite well from sewage in WWTP (Kümmerer, 2009b), the treatment is often not adequate for the removal of antimicrobial resistance genes (ARGs) that are release into the environment, primarily through direct discharges to rivers and lakes (Mokracka et al., 2012; Munir et al., 2013). In fact, studies have shown that antibiotics are not completely degraded during the treatment process (Marti et al., 2013). Several studies have demonstrated the presence of antibiotic residues in treated water at concentration of nanograms per liter (Andreozzi et al., 2003; Janzon et al., 2005; Zhang et al., 2011), including non-biodegradable compounds such as erythromycin, clarinthromycin, amoxicillin, and sulfamethoxazole (Monteiro et al., 2010). Although antibiotics are diluted at concentrations below the minimum inhibitory concentrations (MIC) on ceriches the river might apply a pressure to the development of resistant bacteria (Marti et al., 2013). Additionally, process treatments in the WWTP may also affect to emerge ARB. Treatments such as chlorination may lead to impairment to the microbial populations of WWTP, with the selection of bacteria resistant to chlorination (e.g., *Bacillus subtilis* and *Bacillus liceniformis*), which in turn, contribute to the particular selection of resistant genes (Macauley et al., 2006; Baquero et al., 2008). However, several treatments are effective to treat the antibiotics pollutants. In a conventional wastewater treatment, which includes mechanical treatment, sedimentations, and biological treatment, may eliminate around 80% of the fluoroquinolones or tetracyclines before entering rivers (Sukul et al., 2007; Gulkowska et al., 2008; Baquero et al., 2008). Indeed, some authors have demonstrated that the adsorption, biodegradation, disinfection and membrane

separation are the best routes for removal of antibiotics in water treatment process (Zhang et al., 2011; Golet et al., 2003; Kim et al., 2005), including antibiotics such as ampicillin, norfloxacin, ciprofloxacin, ofloxacin, tetracycline, roxithromycin and trimethoprim (Zhan et al., 2011). Water disinfection with  $\text{ClO}_2$  may contribute to removal of  $\beta$ -lactam agents (Baquero et al., 2008). Applications of techniques such as coagulation, granular activated carbon, and ion treatment are promising approaches for the removal of sulfonamides (Baquero et al., 2008; Choi et al., 2008). Nevertheless, antibiotics and compounds cannot be completely eliminated and enter the environment through sewage sludge and effluents. Distribution and fate of pharmaceuticals are dependent on a range of factors, such as the physico-chemical properties of the drug (e.g., polarity and water solubility), several processes such as partitioning to soil and sediments, and degradation in the aquatic and soil environment (Boxall et al., 2004; Daughton and Ternes, 1999), as well as, environmental characteristics, such as climate and soil type (Boxall et al., 2004; Monteiro et al., 2010).

### **Antibiotic resistance bacteria on biofilms**

Bacteria use different pathways to become resistant to antibiotics, biofilms is one of them. In biofilms, single-celled individuals gather together to form a sedentary but dynamic community within a complex structure, displaying spatial and functional heterogeneity (Bordi and de Bentzmann, 2011). The biofilms are composed of bacterial cells embedded in a complex, self-produced polymeric matrix, in which the cells may be attached to biotic or abiotic surfaces, and differ radically from planktonic cells. Biofilms have been described as being present in most bacterial habitats both in the environment and in the

human body, and they are highly relevant in clinical settings where they cause many types of chronic infections (Stoodley et al., 2002; Burmølle et al., 2014).

Biofilm formation is induced by a variety of stresses, including nutrient limitation, iron limitation, and cell envelope stress. In turn, the biofilm phenotype functions as a barrier that provides protection against environmental stresses (Grant and Hung, 2013). Resistance to antimicrobial agents is the most important cause of non-effective therapy of biofilm associated infections (Ciofu and Tolker-Nielsen, 2011; Marcinkiewicz et al., 2013). The increase in resistance exhibited by bacteria in biofilms can be profound, rendering the cells 10–1,000 times less susceptible to specific antimicrobial agents compared with bacteria in planktonic cultures (Maddox, 2011). This phenomenon is called as biofilm-associated resistance. For example, Archambault and cols (2012) reported that the bacteria *A. pleuropneumoniae* in a biofilm were 100 to 30,000 times more resistant to antimicrobials than their planktonic counterparts. These bacterial biofilms found in natural and pathogenic conditions are formed in the presence of multiple species and genetically distinct strains (Pereira et al., 2010). In general, the increased resistance of bacteria is due to: 1) difficulty of diffusion of antibiotics in to them and electrostatic charge of the exopolysaccharides which attract oppositely charged antibiotics; 2) a low growth rate; 3) changes in phenotype acquired by bacteria forming biofilms; and, 4) inactivation of antibiotics by polymers and enzymes secreted by bacteria (Figure 3). Bacteria in biofilms are also resistant to antibiotics, bactericidal enzymes and disinfectants, such as hypochlorite and glutaraldehyde (Loera-Muro et al., 2008; Loera-Muro et al., 2012). Moreover, biofilms are uniquely suited for horizontal



gene transfer because they sustain high bacterial density and provide a stable physical environment with cell–cell contact (Hannan et al., 2010; Burmølle et al., 2014). Horizontal gene transfer through conjugation and transformation occurs often in biofilm. The large amount of extracellular DNA (eDNA) in biofilms is likely to be an important common source of usable genetic information for members of the biofilm community (Jakubovics et al., 2013; Burmølle et al., 2014). For example, the tetracycline resistance determinant (TetM) has been shown to be spread among different bacteria within oral biofilms by transformation (Burmølle et al., 2014). In natural aquatic environments, outside animal host, it have been found the presence of pathogenic bacteria species forming biofilms, such as *Pseudomonas aeruginosa*, *Vibrio cholera*, and *Mycobacterium ulcerans* (Hall-Stoodley et al., 2005). Moreover, important waterborne bacterial pathogens which can infect the gastrointestinal tract of humans and warm-blooded animals such as *Salmonella enteric*, *Shigella spp.*, *Vibrio cholera*, pathogenic *E. coli* variants, *Yersenia enterocolitica*, *Campylobacater spp.*, and *Helicobacter pylory* have the potential to become components of microbial communities in water biofilm (Wingender, 2011; Wingender et al., 2011). Biofilm producing bacteria (including pathogens) are an important factor that has to be included in risk assessment applied to water-related pathogens and dispersion or ARGs (Wingender et al., 2011).

### **Surveillance programs and risk assessment**

The potential transmission of antimicrobial resistant bacteria among bacteria and/or their resistance determinants to humans and animals is one of the biggest concerns

worldwide. Many monitoring and surveillance programs of antimicrobial resistance in several sectors have been established throughout the world. Surveillance of antimicrobial resistance tracks changes in microbial populations, permits the early detection of resistant strains of public health importance, and supports the prompt notification and investigation of outbreaks. Surveillance findings are needed to inform clinical therapy decisions, to guide policy recommendations, and to assess the impact of resistance containment interventions. The World Health Organization (WHO) recently announced a suite of policies that, if implemented, should mitigate the emergence and further dissemination of antibiotic resistant organisms (Leung et al., 2011). These initiatives have focused on antibiotic stewardship in the hospital and community settings, and reducing antibiotic use in livestock production (Finley et al., 2013). The European Antimicrobial Resistance Surveillance System (EARSS) provide data on antimicrobial resistance for public health purposes ([http:// www.ecdc. europa.eu/en/ activities/ surveillance /EARS- Net/Pages /index. aspx](http://www.ecdc.europa.eu/en/activities/surveillance/EARS-Net/Pages/index.aspx)).

In North America, Canada has the Canadian Integrated Program on The Antimicrobial Resistance Surveillance (CIPARS) that aims to provide information of organisms and environment with antimicrobial resistance in humans, animals and outbreaks of infection due to the same(<http://www.phac-aspc.gc.ca/surveillance-eng.php>). In United States, the National Antimicrobial Resistance Monitoring System (NARMS) is the national public health surveillance system that tracks antibiotic resistance in foodborne bacteria at collaboration with the U.S. Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), and the U.S. Department

of Agriculture (USDA). NARMS monitors antimicrobial susceptibility among enteric bacteria from humans, retail meats, and food animals. NARMS also collaborates with antimicrobial resistance monitoring systems in other countries, to work towards international harmonization of testing and reporting (<http://www.fda.gov/animalveterinary/safetyhealth/antimicrobialresistance/nationalantimicrobialresistancemonitoringsystem/default.htm>). In Latin America, the SENTRY program is responsible for monitoring important pathogens and antimicrobial resistance patterns of nosocomial and community-acquired infections. This program integrates a wide network of information from various hospitals geographically distributed throughout Latin America (Sader et al., 2001). Other countries such as France, Denmark, Spain, Germany, Norway, Italy, Japan, Netherlands, Sweden, Greece, Finland, and Australia also counts with surveillance and monitoring national systems. All the surveillance systems aimed to reduce the antimicrobial resistance spread and the eliminated the generation of new antimicrobial resistance determinants. It is imperative that we obtain better information of the sources, fate and effects of both antibiotics and resistant bacteria in the environment in order to warranty the proper risk assessment and risk management. The emission of antibiotics into the environment should be educed as an important part of the risk management. For this reason, not used therapeutic drugs must to be discarding in proper containers.

Physicians must be made aware that antibiotics are not completely metabolized by patients (humans/animals) and ensure the best practice in prescription of antibiotics and the use of degradable pharmaceuticals instead persistent ones. Antibiotics have to be not able to use as growth promoters or at

less been regulated and limited. Routine analyses of soil and water have to integrate the detection of antibiotics in the environment, and new technologies to investigate the detection, transport, fate on the environment of ARGs, management and removal of these pollutants must be developed, such as ozonation and membrane technology for removal of ARB, multiplex polymerase chain reaction (PCR), real-time PCR, DNA sequencing, and hybridization-based techniques including microarray (Hamelin et al., 2006, 2007; Zhang et al., 2009; Wellington et al., 2013). The improvement of policies to reduce the release of antibiotics and bacteria by anthropogenic ways is also essential. Education to the public on the importance of antibiotics and the prudent use and disposal of the antibiotics has to be made. Surveillance programs are need it worldwide and even more in developing countries were wastewater treated represents often the main source of water to food irrigation. Wastewater treatment plants have to be considerate as biological reactors for antibiotic resistant spread and where horizontal transfer often occurs (Kümmerer, 2003).

Dedicated hospital wastewater treatment must be exists. We also need to take in consideration that the use of one antibacterial agent can increase levels of multiple drugs, and not only to a specific one (cross-resistance), and transfer of resistance genes is most likely to occur in compartments with high bacterial density like in biofilms (Kümmerer, 2009). A corresponding metric for environmental antibiotic concentration could be developed based on the concept of the minimum selective concentration (MSC) (Gullberg et al., 2011), defined as the minimum concentration of an antibiotic agent that selects for resistance (Liu et al., 2011).

Management of wastewater treatment must consider the antibiotics as micropollutants in order to reduce the promotion of emergence of antibiotic resistant bacteria.

## **Conclusion**

Aquatic environments are one of the mainways to spread and evolution of antimicrobial resistant bacteria. In water, especially with high density of microorganisms, bacteria of different species and from diverse origins are mixed and given arise to new antimicrobial resistant strains due to the genetic exchange between different bacterial species. All together, resistant bacteria release in the environment directly from the human and animal treated with antibiotics increase the prevalence of resistant strains. Furthermore, antibiotics, quaternary ammonium compounds, health care products and heavy metals could increase the selection of antimicrobial resistant bacteria and reduce the susceptible microbiota in the environment. Pollution by antibiotic and their determinants can enhance the possibilities of human pathogens for acquiring resistance. Several efforts have to be made in order to reduce the impact of antibiotics in the environment and public health. To reduce the impact of resistance genes containment measurements avoiding as much as possible the contact of human-linked and environmental bacteria should be evaluated (Baquero et al., 2008; Martínez et al., 2009). New policies has to be made for limiting the use and misuse of antibiotics as well as limiting the use as growth promoters in farming animals. Water quality assessment must integrate detection of antibiotics in water as a routine quality parameter. New guidelines for treatment water must to be made in order to include the management of antibiotic bacteria and resistance genes in wastewater and detection

and removal of these pollutants. The dispersal of bacteria may contribute to the storage and dissemination of antibiotic resistance genes in the environment, for this reason it should has a better handle in both wastewater treatment plants and anthropological activities to control and even eradicate such dispersion and ensuring effective treatment against infectious diseases.

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