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Emergence of Antibiotic Resistant Bacteria from Coastal Environment – A Review

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1. Introduction

Antibiotic resistance in microbes is a growing issue of human health. The extraordinary ability of microbes to develop resistance to various antibiotics attracted evolutionary scientists and environmental biologists in recent years. Historically, the use of antimicrobial agents started in 1904 with the discovery of Tripan red by Ehrlich and Shiga (Browning & Gulbransen, 1936). In 1929, penicillin was discovered by Alexander Fleming when his group found that the fungus *Penicilium notatum* produces a very selective inhibitor for *Staphylococcus* sp. Fleming's discovery showed that not only synthetic agents like Ehrlich's "Magic Bullet" but also a microbial product can be an effective antimicrobial drug (Hare, 1970). In 1943, Waksman started to use the word "antibiotics" when he discovered streptomycin (Wainwright, 1988). After the initial age of discovery and since the 1970s many antimicrobial agents have been developed together with the discoveries of new antibiotics. It is well documented that the evolution of antibiotic resistance in bacterial strains is a direct consequence of natural selection applied by widespread use of antibiotic drugs (Benveniste & Davies, 1973). The providential experiment by Fleming demonstrated the production of antibiotics (Penicillin) which eventually led to its large-scale production from mold *Penicillium notatum* in the 1940s. As early as the late 1940s resistant strains of bacteria began to appear due to their extraordinary ability in gaining resistance towards any particular antibiotics with elapsing generation (Shoemaker et al., 2001; Chopra & Roberts et al., 2001; Doern et al., 2001). In 1980 it was estimated that 3–5% of *S. pneumoniae* were penicillin-resistant and by 1998, 34% of the *S. pneumoniae* sampled were resistant to penicillin. Currently, it is estimated that more than 70% of the bacteria that cause hospital-acquired infections are resistant to at least one of the antibiotics used to treat them (NIAID, 2006).

Antibiotics are defined as a chemical substance derived from microorganisms, which have the capacity to inhibit growth, and even destroying other microorganisms in a dilute solution (ICON, 2003). Antibiotics are low-molecular-mass (<1500 kDa), products of secondary metabolism and nonessential for the growth of producing organisms, but are

very important for human health. They have unusual structures and are most often formed during the late growth phase of the producing microorganisms. These secondary metabolites have exerted a major impact on the control of infectious diseases and other medical conditions, and the development of pharmaceutical industry. Their use has contributed to an increase in the average life expectancy in the USA, which increased from 47 years in 1900 to 74 years (in men) and 80 years (in women) in 2000 (Reynolds, 2010). Probably, the most important use of secondary metabolites has been as anti-infective drugs. In 2000, the market for such anti-infectives was US$55 billion and in 2007 it was US$66 billion, with the estimated global antibiotic consumption of between 100,000 and 200,000 tonnes per year (Demain & Sanchez, 2009).

Coastal environment plays a very important role as habitat to a number of plants and animals. They serve as breeding and nursery grounds, shelters, sources of food for various marine lives. In the recent times, pollution of coastal areas represents one of the most important environmental problems because it causes economic and tourism damages as well as affects health quality. It was noted that antibiotics released into the aquatic environment are of great concern for the three important reasons: (1) Contamination of water used for drinking, irrigation and recreation, (2) Widespread occurrence of bacterial resistance to antibiotics, and (3) Negative effect on microbes which play vital role in nutrient cycling (e.g. nitrogen cycle) and regeneration of nutrients in aquatic ecosystems (Costanzo et al., 2005). The use of antibiotics is the main treatment applied to control bacterial illness in fish farms (Castro et al., 2008). Due to the use of a wide variety of antibiotics, aquaculture has been implicated as potential environment to the development and selection of resistant bacteria and a source of these pathogens to other animals and humans (Hatha et al., 2005; Serrano, 2005). It has also been noted that sediment samples containing microorganisms with antibiotic resistance alter the production of β-lactamase in the human defence system (Lu, et al., 2010). The issue of antibiotic resistance was extensively addressed in the scientific literature describing the presence of antibiotics in the environment (e.g. Nygaard et al., 1992; Samuelsen et al., 1992). But, a comprehensive review on the emergence of antibiotic resistance strains from the aquatic habitat is still scanty.

3. Antibiotic resistance an ecological perspective

Although antibiotics have been used in large quantities for some decades, until recently the existence of these substances in the environment has received little attention. It is only in recent years that a more complex investigation of antibiotic substances has been undertaken in order to permit an assessment of the environmental risks (Kümmerer, 2009a & b). Within the last decade, an increasing number of studies covering antibiotic input, occurrence, fate and effects have been published (Kümmerer, 2009 b; Björkman et al., 2000; Alanis, 2005). Antibiotic resistance is one of the major challenges for human medicine and veterinary medicine. However, there is still a lack of understanding and knowledge about sources, presence and significance of resistance of bacteria against antibiotics in the aquatic environment despite the numerous studies performed (Kümmerer, 2009b).

Antibiotic resistance can reach the environment with the potential of adversely affecting aquatic and terrestrial organisms which eventually might reach humans through drinking water and food chain (Edquist & Pedersen, 2001; Prior, 2008; Aarestrup et al., 2008). The history of resistance due to the use of antibiotics has only recently been described in more

detail (Edquist & Pedersen, 2001; Prior, 2008). In general, the emergence of resistance is a highly complex process which is not yet fully understood with respect to the significance of the interaction of bacterial populations and antibiotics, even in a medicinal environment (Björkman et al., 2000; Martinez & Baquero, 2000; Alanis, 2005). The transfer of resistant bacteria to humans could occur via water or food if plants are watered with surface water or sewage sludge, if manure is used as a fertilizer, or if resistant bacteria are present in meat (Perreten et al., 1997; Khachatourians, 1998; Dolliver & Gupta, 2008). The significance of the transfer of antibiotic resistance from animals to humans is not clearly understood. However, to minimize this route and the unwanted intake of antibiotics, the antibiotic content of fishery products is monitored by authorities in many countries (WHO, 2003; IM, 1989; FAAIR, 2002).

Many bacterial species multiply rapidly enough to double their numbers every 20–30 minutes, therefore, their ability to adapt to changes in the environment and survive unfavorable conditions often results in the development of mutations that enable the species to survive in changing external conditions (Ferenci, 2008). Research on the use of antibiotics in aquaculture shows similar results with the medical use of antibiotics (Weston, 1996). The important research findings in this regard are: (1) The use of one antibacterial agent can increase levels of resistance not only to that specific drug but also to many others, even those using very different modes of antibacterial action (cross-resistance). (2) Antibacterial resistance does not always respond in a predictable fashion correlating with the amount of drugs used or with the concentrations of residues in the environment (Hernando et al., 2006).

3.1 Coastal environment

Coastal Environment plays a very important role as habitat to a number of microbes, plants and animals. They serve as breeding grounds, shelters, sources of food for marine life, and are home to a number of endangered species (Kuijper, 2003). Over half of the current global population lives within 200 km of the coastline. For the future, the Centre for Climate Systems Research (CCSR) of the Earth Institute at Columbia University estimates a strong growth of coastal population by 2025. The coastal zone contains natural systems that provide more than half of the global ecosystem goods (e.g., fish, oil, minerals) and services (e.g., natural protection from storms and tidal waves, recreation). In addition, 14 of the world's 17 largest megacities are located along coasts and most of them are located in Asia's fastest growing economies (www.loicz.org). The overcrowding of beaches has led to large-scale destruction of some of these habitats and has reduced their ability to adapt to drastic environmental changes. Development, climate change, and commercialization have all contributed a major part in increasing the pressure on beach ecosystems. Besides this fact, anthropogenic input of various pollutants especially antibiotics into the aquatic environment has increased the resistant capacity of the bacterial strains. In general, bacterial load is higher in the sediments compared to the overlying water body. Hence, more investigations were carried out on surface soil samples (Jensen et al., 2001; Tolls, 2001; Marengo et al., 1997. It has been noted that persistence of antibiotics in soil depends on many factors including soil type, climate, and class of antibiotics (Bonaventura, 2004). Most antibiotics are recycled in soils through natural cycles but some of them have a long half-life (Kumar et al., 2005; Kümmerer, 2009a). According to Marengo et al. (1997), less than 1% of

sarafloxacin, an antibiotic used widely in poultry production, degrades in the soil after 80 days of incubation. These antibiotics may leach to ground water or move to surface waters via surface runoff. Olapade et al., (2006) have reported that these antibiotics find their way to the coastal and marine environment.

Antibiotics have both quantitative and qualitative effects on the native microbial communities in soil environment (Nygaard et al., 1992). Although antibiotic concentrations in most soils are not at therapeutic levels to cause inhibitory effects on bacterial population, it may still influence the selection of antibiotic resistant bacteria in the niche (USEPA, 2002). Jensen et al. (2001) have recorded an increased antibiotic resistance among *Pseudomonas* sp. and *Bacillus cereus* after exposure to soil sediments. Many antibiotics have a strong tendency to bind with soil particles (Tolls, 2001; Kummerer et al., 2003). Distribution coefficients ($K_{d,solid}$) as high as 2300, 6310, and 128 L kg^{-1} have been reported for tetracycline, enrofloxacin, and tylosin, respectively (Kummerer et al., 2003). Our research team has earlier shown that the bacterial isolates from the tropical mangrove sediments are 100% resistant against β - lactam antibiotics (ampicillin, amoxicillin and penicillin). Bacterial isolated from mangrove sediment soil have exhibited 66.7 and 77.8% resistance against chloramphenicol and streptomycin, respectively, suggesting that the lipid composition may play a key role in preventing the entrance or binding of antibiotics to the cell (Jalal et al., 2010). Interestingly, All the isolates are susceptible to ciprofloxacin since it inhibits the enzyme topoisomerase II that causes the negative super-coil in DNA strands and thus permits transcription or replication. All the bacterial isolates display Multi Antibiotic Resistance (MAR) index higher than 0.2 indicating the high-risk sources of contamination in the environment (Jalal et al., 2010).

3.2 Aquaculture

In aquaculture fields, high loads of antibiotics in sediments at concentrations potent enough to inhibit the growth of bacteria have been reported (Costanzo et al., 2005; Hatha et al., 2005; Hirsch et al., 1999; Holmström et al., 2003; Kümmerer, 2009a &b). Resistant bacteria may be present in sediments because of the application of antibiotics in fish farming or because of selection through the antibiotics present in the sediments. The fact that the exposure is highly concentrated must also be considered to be critical. The substances used in fish farming can enter sediments directly from water without undergoing any kind of purification process. Some investigations have demonstrated the presence and persistence of antibiotics applied extensively in fish farming in sediments beneath fish farms (Kümmerer, 2003). Fluoroquinolones, sulphonamides and tetracyclines are strongly adsorbed (Kümmerer, 2009b) and therefore, they can readily accumulate in the sediments. It is not clearly known as to what degree and under what circumstances the compounds are effective after sorption or whether they are released to contribute to resistance. Antimicrobials can have qualitative and quantitative effects upon the resident microbial community in sediments. In the fish farming sector (aquaculture, mariculture, etc.), the widespread use of antibiotics for treating bacterial diseases is associated with the development of antibiotic resistance in *Aeromonas hydrophila, Aeromonas salmonicida, Edwardsiella tarda, Edwardsiella icttaluri, Vibrio anguillarum, Vibrio salmonicida, Pasteurella piscida* and *Yersinia ruckeri* (Serrano, 2005). Bacteria resistant against these compounds have been detected in sediments. Increased antibacterial resistance in sedimentary bacteria is often the most sensitive

environmental indicator of past antibacterial use (Kümmerer, 2003). Various patterns of resistance among strains were isolated from very close geographical areas during the same year, suggesting diverse patterns of drug resistance in environmental bacteria within this area. In addition, the cross-resistance patterns have suggested that the resistance determinants among *Vibrio* spp. are acquired differently within sediment and seawater environments (Neela et al., 2007).

As far as intensive shrimp culture goes, a large amount of shrimp food and antibiotics have been used to increase production and to protect shrimp from diseases (EJF, 2003). Consequently, a large portion of feeds and antibiotics enters the water as wastes, causing water pollution (Le et al., 2003). Several studies have demonstrated the presence of antibacterial residues in fish farms (Weston, 1996; Capone et al., 1996; Herwig et al., 1997). Recent studies have shown that many antibiotics persist in the sediment and in the aquatic environment for several months following administration (Bjorklund et al., 1991; Lai et al., 1995; Pouliquen & Le, 1996; Hirsch et al., 1999; Miranda & Zemelman, 2002).The residues of antibacterial agents may affect the sedimentary microbial community and introduce antibiotic resistance in the bacteria (Hektoen et al., 1995; Tendencia & Dela Pena, 2002). Mc Phearson et al. (1991) have observed that individual and multiple antibiotic resistances are associated with antimicrobial use. A study in Thailand has indicated that the pattern of antibiotic use among the farms can cause the risk of the development of resistant bacteria strains (Holmostro¨m et al., 2003). Little is known about the occurrence of antibiotic resistant bacteria in marine sediments near fish farms (Schmidt et al., 2000; Tendencia & DelaPena, 2001).

4. Antibiotic resistance in sea food

Sea foods are often susceptible to spoilage by putrefactive microorganisms. Sea foods usually spoil much more rapidly than meats obtained from warm blooded animals when stored at ordinary refrigerator temperatures, and the reason for this is almost certainly because of the marine products that are invariably contaminated with psychrophilic bacteria (Witter, 1961). These organisms not only multiply quite rapidly at refrigerator temperatures, but spoil fish about twice as fast at 37^0 F as at 30^0 F (Bluhm et al., 1956). Though proper vessel and fish plant sanitation are obviously highly desirable for production of high quality fish, it is quite possible to prepare fish of excellent bacteriological quality in quite primitive premises. In other words, the maintenance of high sanitary standards on fishing vessels and at shore plants does not necessarily insure good quality fish, though from an aesthetic stand point alone such conditions are highly desirable. It is the actual handling and treatment of the fish themselves which is of prime importance in determining their quality.

Reviews and original articles dealing with antibiotics in fish or shellfish preservation have been published from other laboratories (Tomiyama et al., 1955; Ingram et al., 1956). Antibiotics have been commonly used to preserve the fish from bacterial contamination. In 1943 penicillic acid was prepared and tested as a possible preservative for fish with poor success (Tarr, 1944). Later penicillin and streptomycin were examined with similar disappointing results (Tarr, 1948). In the spring of 1950, a number of the newer antibiotics were studied and the findings were much more encouraging since Aureomycin, Terramycin and Chloromycetin all gave quite significant preservation in comparatively low concentration (Boyd & Tarr, 1956). Further experiments proved that of 14 antibiotics

examined, Aureomycin (chlortetracycline, CTC) was found most effective (Tarr et al., 1954) and it is with this antibiotic that all applied studies have been conducted (Gillespie et al., 1955; Steiner and Tarr, 1955; antibiotics as food preservatives; Tarr et al., 1954).

Effect of several new antibiotics and furan derivatives on growth of bacteria in fish products have been studied and they are: (1) Antibiotics: Aureomycin (Lederle Laboratories), Amphomycin, Etamycin, Bryamycin (Bristol Laboratories, Inc.); and (2) Furan derivatives: Furoxone, Furadantin, Nitrofurazone (Furacin), and N. F. 56 (N-5-nitro-2 furfurylidene-l-aminoguanidine sulphate) (Eaton Laboratories, Inc.) (**Table 1**). The technique is similar to that employed in previous studies with ground flesh (Tarr et al., 1950).

Compound	concentration (µg/g)	Bacterial counts (colony forming units × 10^6/g) at temperature			
		1^0C		5^0C	
		6	8	6	6
None		27	>600	600	130
Aureomycin (CTC)	2.5	1.3	0.5	7	19
Amphomycin	5			450	
Bryamycin	5				98
	10	92	340		
	20	19	470		
Etamycin	5		910		
	10		380		
Furoxone	2.5				32
Furadantin	2.5				85
Nitrofurazone	2.5				114
	10	37	>900		
	25	57	310		
	50	19	900		
NF-56	2.5				63
	25	157	837		
	50	76	367		
CTC+ Bryamycin	5				
	10	2.7	8		
CTC+ Bryamycin	2.5				
	5	4	1		
NF-56+ Bryamycin	25		>900		
	10				
Nitrofurazone+ Bryamycin	25				
	10	18	400		

Table 1. Effect of various antibiotics and Furan derivatives on growth of bacteria in Minced Lingod muscle at 0^0 and 4^0C (Boyd et al., 1955).

The search for antibiotics or other substances which could prove valuable in preventing microbiological spoilage of fish or fish waste products is continuing, and the results of trials with several new antibiotics and furan derivatives are presented. It has been argued that suppression of natural bacterial flora of fish by introduction of CTC might create favorable conditions for the growth of food poisoning microorganisms.

5. Antimicrobial resistance in drug development

5.1 Mechanism of antibiotic resistance in bacteria

A key factor in the development of antibiotic resistance is the ability of infectious organisms to adapt quickly to new environmental conditions. Bacteria are single-celled organisms that, compared with higher life forms, have small numbers of genes. Therefore, even a single random genetic mutation can greatly affect their ability to cause disease. And because most microbes reproduce by dividing every few hours, bacteria can evolve rapidly. A mutation that helps a microbe surviving to an antibiotic exposure will quickly become dominant throughout the microbial population. Microbes also often acquire resistance genes from each other through horizontal gene transfer mechanism which might enable them to be a multiple antibiotic resistant strain. It is also noted that the specificity of the interactions between antibiotics and various protein sequences within a bacterium resultse in significantly high ratio of mutations in its genome which leads to antibiotic resistance. There is also a relatively high possibility that a particular mutation in a certain target sequence will result in antibiotic resistance.

Antibiotics generally target a variety of essential bacterial functions. For instance, the β-lactam antibiotics and vancomycin interrupte cell wall synthesis of pathogens, whereas macrolides and tetracyclines disrupt the protein synthesis at ribosomal level. Bacteria may develop their antibiotic properties by a variety of mechanisms. According to a study by Nicolaou (2001), one mechanism of resistance is by degrading the antibiotic in a step by step process. This degradation starts when bacterial β-lactamases hydrolyzes the β-lactam ring thus rendering these antibiotics ineffective. A secondary resistance mechanism is then triggered when the antibiotic target is altered. As the next step, bacteria may block the entry of antibiotic to the site of action, resulting in decreased absorption, which in turn results in bacteria with decreased sensitivity to vancomycin due to thicker cell walls. Finally, bacteria may develop efflux pumps that actively pump antibiotics out of the cell so that they do not reach their target. Nicolaou also tested the findings experimentally with macrolides and has found that if the ribosomal binding site for macrolides changes so that these antibiotics bind with decreased affinity, then protein synthesis will not be disrupted.

5.2 Drug discovery

When bacteria contact with chemical substances, they show a positive or negative chemotaxis. If the substrates are acceptable for bacteria or can support bacterial growth, they show a positive chemotaxis and utilize the substrate as an organic source. If toxic, they respond by escaping from the chemical(s). Antibiotics selectively inhibit bacteria based on targeting a specific structure or function of bacteria, which means antibiotics act as toxins to bacteria. Mostly the targets of antibiotics are prokaryote-specific mechanisms and structures, which are not present in eukaryotes or they have different characteristics from those of

eukaryotic cells. However, bacteria inherently have potential drug resistance mechanisms or they can acquire exogenous genes conferring drug resistance. Drug resistance therefore, occurs by such mechanisms. At present, four main categories of drug resistance mechanisms are known (Li & Nikadio, 2009). They are: (1) Drug inactivation or modification: for example, enzymatic deactivation of *Penicillin* G in some penicillin-resistant bacteria through the production of β-lactamases, (2) Alteration of target site: for example, alteration of PBP—the binding target site of penicillins—in MRSA and other penicillin-resistant bacteria, (3) Alteration of metabolic pathway: for example, some sulfonamide-resistant bacteria do not require para-aminobenzoic acid (PABA), an important precursor for the synthesis of folic acid and nucleic acids in bacteria inhibited by sulfonamides. Instead, like mammalian cells, they turn to utilizing preformed folic acid, and (4) Reduced drug accumulation: by decreasing drug permeability and/or increasing active efflux (pumping out) of the drugs across the cell surface (Li & Nikadio, 2009) .Some of these mechanisms have been well studied at the molecular level (Walsh, 2003).

The integrated approaches for maximizing the diversity of microbes in drug discovery programs have been reviewed recently, with selective isolation of novel microorganisms (Knight et al., 2003; Zhang et al., 2005; Bian et al., 2008; Wagner-Dobler et al., 2002). Recently Cubist Pharmaceuticals has constructed a multi-drug resistant *E. coli* strain, which carries resistance markers for 17 of the most frequently produced antibiotics. Thus, a comparison of extract activities against sensitive and resistant *E. coli* strains will allow researchers to rapidly discovering novel and specific active compounds that can be used as effective drugs against pathogenic strains (Baltz, 2008). From these studies, it is strongly anticipated that metagenomic libraries of the drug resistant microbial strains will drive drug discovery process now and in the future. Hence, undoubtedly, metagenome analysis technology combined with high throughput screening will bring innovation to the drug discovery.

6. Impact of antibiotic resistance on human health

It has been widely understood that the bacteria and other microorganisms that often cause infections are known to be remarkably resilient and have the ability to develop ways for surviving drugs that are meant to kill or weaken them. Recent scientific evidence suggests that during the last decade, antibiotic resistance by various mechanisms has increased worldwide in bacterial pathogens leading to treatment failures in human and animal infections (Singer et al., 2003). However, the resistance against different types of biocides (including disinfectants, antiseptics, preservatives, sterilants) has been studied and characterized (Russell, 1990 & 1995). Only limited sound scientific evidence to correctly assess the risks of antibiotic resistance induced by resistance to biocides is available (SCENIHR, 2009). Furthermore, research indicates that biocides and antibiotics may share some common behaviour and properties in their respective activity and in the resistance mechanisms developed by bacteria (Russell, 2003, Sheldon 2005).

Although antibiotic usage has clearly benefited the animal industry and helped providing affordable animal protein to the growing human population, the use of antibiotics in food production has also contributed to the emergence and spread of antibiotic multiple resistance (AMR). Along with antibiotics used for human medicine, the use of antibiotics for animal treatment, prophylaxis and growth promotion exerts an inestimable amount of selective pressure toward the emergence and propagation of resistant bacterial strains.

Animals can serve as mediators, reservoirs and disseminators of resistant bacterial strains and/or AMR genes. Consequently, imprudent use of antimicrobials in animals may eventually result in increased human morbidity, increased human mortality, reduced efficacy of related antibiotics used for human medicine, increased healthcare costs, increased potential for carriage and dissemination of pathogens within human populations and facilitated emergence of resistant human pathogens (**Figure 1**).

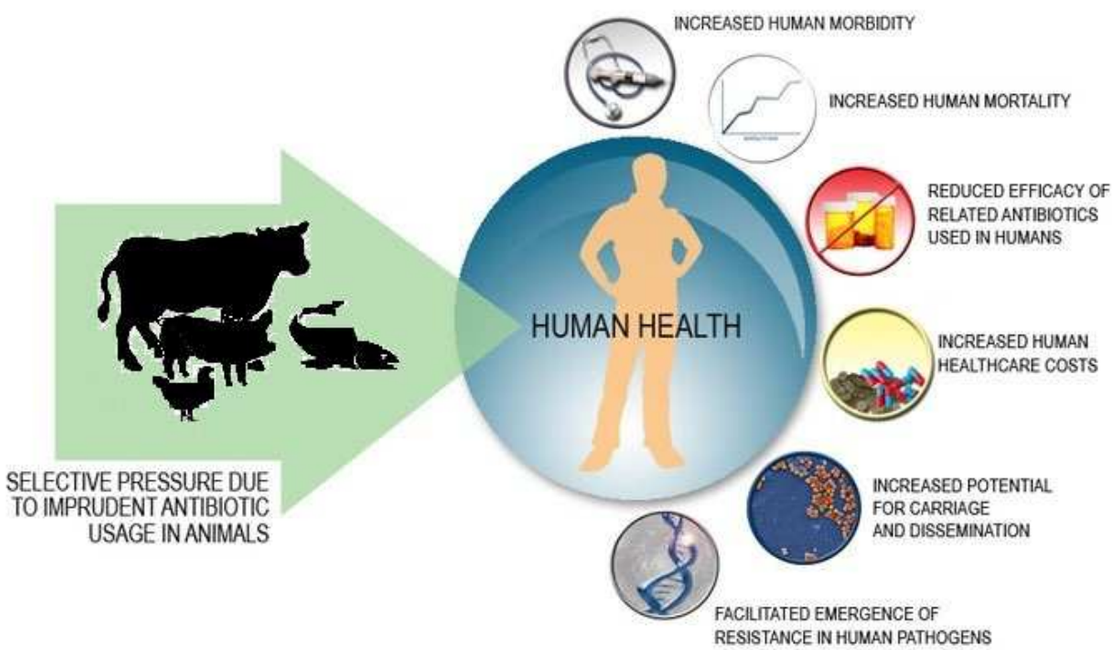

Fig. 1. The Human Health Impact of Antimicrobial Resistance in Animal Populations

According to Helms et al., (2002), the patients infected with pansusceptible *Sal*monella typhimurium are 2.3 times more likely to die within 2 years after infection than persons in the general Danish population, and that patient infected with strains resistant to amplicillin, chloramphenicol, streptomycin, suldonamide and tetracycline are 4.8 times (95% CI 2.2 to 10.2) more likely to die within 2 years. Furthermore, they have established that quinolone resistance in this organism is associated with a mortality rate 10.3 times higher than the general population.

It has been well documented that antimicrobial resistance due to a particular antibiotic used in food animals may result in reduced efficacy of most or all members of that same antibiotic class, some of which may be extremely important for human medicine (McDonald et al., 2001). The current pharmaceutical era faces multi resistant infectious disease organisms that are difficult and, sometimes, impossible to treat successfully. When there is an increase in numbers of bacteria that are resistant to antibiotics, it will be more difficult and more expensive to treat human bacterial infections. According to a study published by the Centers for Disease Control and Prevention (CDC), up to date, there are more than 100 antibiotics approved by the US Food and Drug Administration for human use. As antibiotics fail to treat recurring infections, the consequences include frequent visits to the doctor, hospitalization or even a need for a more expensive medication as a replacement for the

existing ineffective ones (Levy, 2002). Increased healthcare costs are another important consequence of antimicrobial resistance. Increased costs are due to the need for additional antibiotic treatments, longer hospitalization, more diagnostic tests, higher professional costs and more pain management. In 1998, the Institute of Medicine estimated the annual cost of infections caused by antibiotic-resistant bacteria at US$ 4 to 5 million per year (McGowan, 2001). This occurrence of antibiotic resistance is found all over the world and has become a very serious problem in the treatment of diseases. The US Office of Technology Assessment report has attributed a cost of $1.3 billion per year for antibiotic-resistant infections in US hospitals. The fiscal cost of treating antibiotic resistant infections worldwide has been estimated to be many billions of dollars per year.

7. Conclusion

At present, there is insufficient information available to reach a final conclusion on the significance and impact of the presence of resistant bacteria in the environment which would allow the assessment of the potential risks related, for instance, to human health and ecosystem functions. Currently, it is thought that the input of antibiotics in general as well as from hospitals seems to be of minor importance, at least in terms of resistance. Up to now, antibiotics have not been detected in drinking water. The impact of antibiotics present in the aquatic environment on the frequency of resistance transfer is questionable. The information available to date suggests that the input of resistant bacteria into the environment from different sources seems to be the most important source of resistance in the environment. Therefore, the prudent use of antibiotics and disinfectants will significantly reduce the risk for the general public and for the environment. This not only means limiting the duration of selective pressure by reducing the treatment period and the continuous use of sub-therapeutical concentrations, but also includes controlling the dissemination of antibiotics being used, as well as prudent monitoring of resistance. However, a full environmental risk assessment cannot be performed on the basis of the data available; the availability of such data is a prerequisite if proper risk assessment and risk management programs for both humans and the environment are to be undertaken. Therefore, the careful use of antibiotics and the restriction of their input into the aquatic environment are the matters of necessity.

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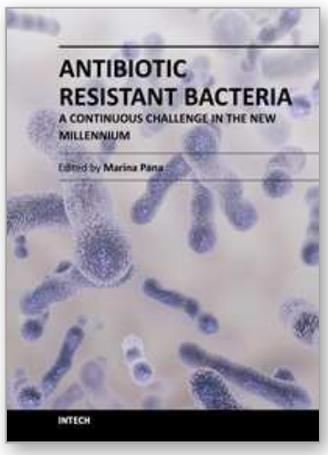

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Antibiotic-resistant bacterial strains remain a major global threat, despite the prevention, diagnosis and antibiotherapy, which have improved considerably. In this thematic issue, the scientists present their results of accomplished studies, in order to provide an updated overview of scientific information and also, to exchange views on new strategies for interventions in antibiotic-resistant bacterial strains cases and outbreaks. As a consequence, the recently developed techniques in this field will contribute to a considerable progress in medical research.

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