Letters in Applied Microbiology

Letters in Applied Microbiology ISSN 0266-8254

REVIEW ARTICLE

The prevalence and antimicrobial resistance phenotypes of *Salmonella*, *Escherichia coli* and *Enterococcus* sp. in surface water

S. Cho, C.R. Jackson and J.G. Frye

Bacterial Epidemiology and Antimicrobial Resistance Research Unit, United States Department of Agriculture, Agricultural Research Service, Athens, GA, United States of America

Significance and Impact of the Study: Surface water is prone to bacterial contamination as it receives wastes and pollutants from human and animal sources, and contaminated water may expose local populations to health risks. Studies have demonstrated the widespread distribution of pathogenic and antimicrobial resistant bacteria in surface waters of both developing and developed countries, confirming the importance of environmental waters as a reservoir for these bacteria and the need for more attention on the environmental bacteria for emerging antimicrobial resistance. This review discusses the prevalence and diversity of pathogenic and commensal bacteria, namely *Salmonella*, *E. coli*, and *Enterococcus*, present in surface waters and provides a basic understanding of the occurrence and persistence of antimicrobial resistance in these bacteria.

Keywords
antimicrobial resistance, *Escherichia coli*, *Enterococcus*, environmental water, prevalence, *Salmonella*, virulence.

Correspondence
Sohyun Cho, Richard B. Russell Research Center, 950 College Station Road, Athens, GA 30605, USA.
E-mail: sohyun.cho@usda.gov

2020/0318: received 21 February 2020, revised 9 April 2020 and accepted 13 April 2020

doi:10.1111/lam.13301

Abstract

Surface water is prone to bacterial contamination as it receives wastes and pollutants from human and animal sources, and contaminated water may expose local populations to health risks. This review provides a brief overview on the prevalence and antimicrobial resistance (AR) phenotypes of *Salmonella*, *Escherichia coli* and *Enterococcus*, found in natural freshwaters. These bacteria are frequently detected in surface waters, sometimes as etiological agents of waterborne infections, and AR strains are not uncommonly identified in both developed and developing countries. Data relating to *Salmonella*, *E. coli* and *Enterococcus* present in environmental water are lacking, and in order to understand their development and dissemination using the One Health approach, understanding the prevalence, distribution and characteristics of the bacteria present in surface water as well as their potential sources is important. Furthermore, AR bacteria in natural watersheds are not well investigated and their impacts on human health and food safety are not well understood. As surface water is a receptacle for AR bacteria from human and animal sources and a vehicle for their dissemination, this is a crucial data gap in understanding AR and minimizing its spread. For this review, *Salmonella*, *E. coli* and *Enterococcus* were chosen to evaluate the presence of primary pathogens and opportunistic pathogens as well as to monitor AR trends in the environmental water. Studies around the world have demonstrated the widespread distribution of pathogenic and AR bacteria in surface waters of both developing and developed countries, confirming the importance of environmental waters as a reservoir for these bacteria and the need for more attention on the environmental bacteria for emerging AR.

Introduction

Surface water and waterborne outbreaks

Surface waters are constantly influenced by human activities as they are used for recreational activities, such as swimming, kayaking, tubing, surfing and fishing, and serve as a receptacle for wastes and wastewater from surrounding wastewater treatment plants, septic systems and industrial facilities. Contaminations by animal wastes can also occur due to runoff from animal farms, wildlife and parks with domestic pets. Since bacterial pathogens present in the gastrointestinal tract of humans and other warm-blooded animals are shed into environmental water, ingestion or contact with contaminated water can lead to infections with primarily gastrointestinal symptoms by the faecal–oral route, and also with respiratory, eye, ear and skin symptoms (DeFlorio-Barker *et al.* 2018). Faecal contamination from various human and animal sources can pose health risks to local populations exposed to environmental water through municipal, agricultural and recreational uses; hence, to reduce the public health risk, monitoring the water for any microbial pollutants is essential.

Waterborne diseases still remain the leading cause of morbidity and mortality worldwide, causing about 2·2 million deaths per year (WHO and UNICEF 2000). In developed countries, improved sanitation and water quality have reduced the number of waterborne infections and the severity of their impacts as compared to developing countries, with some of the fatal waterborne infections such as cholera and typhoid fever considerably reduced in number (WHO and UNICEF 2000; Craun *et al.* 2006; Cabral 2010). However, water-associated outbreaks still occur in developed countries, suggesting the need for attention to water quality (Benedict *et al.* 2017; Graciaa *et al.* 2018; Hlavsa *et al.* 2018). Outbreaks of bacterial diseases associated with contaminated surface water have been frequently reported in North America, responsible for both public health and economic burdens (Olsen *et al.* 2002; Hrudey *et al.* 2003; Beach 2004). During 2000–2014, 140 outbreaks and 4 958 illness cases associated with untreated recreational water, such as lakes and oceans, were reported in the United States alone, and a third of the outbreaks with known aetiology were attributed to bacteria such as *Shigella*, *Escherichia coli* and *Leptospira* (Graciaa *et al.* 2018). While Graciaa *et al.* reported only the identified outbreaks and illnesses, a study conducted by DeFlorio-Barker *et al.* estimated approximately 90 million illness cases, including both sporadic and outbreak cases of all levels of severity, that are associated with surface water recreational activities, such as swimming, kayaking, rowing, canoeing, motor boating and fishing, annually in the United States (DeFlorio-Barker *et al.* 2018; Graciaa *et al.* 2018). This translated into an economic burden of 2·9 billion US dollars, resulting from healthcare provider visit, medication, hospitalization, sequelae, mortality and lost productivity (DeFlorio-Barker *et al.* 2018).

Antimicrobial resistance and the one health approach

Antimicrobials have had a significant impact on treating and controlling bacterial infectious diseases, reducing the burden of illnesses since the 20th century (Aminov 2010). Since the introduction of the first antimicrobial agent approximately seven decades ago, antimicrobials have been widely used in both humans and animals for therapeutic use as well as at sub-therapeutic levels in animals for promoting growth, improving feed efficiency and preventing diseases (Aarestrup and Wegener 1999; Aminov 2010). However, resistance to antimicrobials was detected soon after their introduction to the public, and the overuse and misuse of the drugs have led to a rapid increase in antimicrobial resistance (AR) (Alanis 2005). Resistance to therapeutic antimicrobials is a public health concern as it renders an antimicrobial ineffective whenever treatment is needed and potentially results in treatment failure (Levy and Marshall 2004). The World Health Organization (WHO) has provided a list of critically important antimicrobials in humans and recommended the prudent use of the drugs to prevent the development and dissemination of resistance in pathogenic bacteria, the consequence of which can be severe for human health (WHO 2000; WHO 2019). The Centers for Disease Control and Prevention (CDC) estimates about 2·9 million infections and 35 900 deaths each year due to AR infections in the United States alone (CDC 2019). This is a more serious problem in developing countries where antimicrobials are available without a prescription and their distributions are not effectively regulated (Alanis 2005). If AR were to continue at the same rate with the same trend as now, infections due to AR bacteria are estimated to cost the world 300 million premature deaths and 100 trillion US dollars by 2050 (Resistance 2014). The emergence of bacteria resistant to medically important antimicrobials due to selective pressure created by sub-therapeutic usage in animals has contributed to the transfer of AR bacteria to humans, and in response, the sub-therapeutic use of antimicrobials for growth promotion and disease prevention has been banned or controlled in multiple countries (FDA 2012; Maron *et al.* 2013; Holmes *et al.* 2016).

Antimicrobial resistance has become a threat to the public health worldwide, and the development of effective strategies to combat AR is a global task that needs to be addressed by governments and the public around the

world. The World Health Organization (WHO), along with the Food and Agriculture Organization of the United Nations (FAO) and the World Organization for Animal Health (OIE), has claimed AR as one of the three priority public health threats that needs to be addressed with the help of global collaboration (WHO 2014). To address this challenge and elucidate the emergence, dissemination and fate of AR, the One Health approach has been implemented. One Health approach is defined as collaborative and transdisciplinary efforts working at the local, national and global levels to achieve optimal health for humans, animals and the environment (AVMA 2008). One Health concept, which recognizes that the health of animals, people and the environment is connected, is not a new concept but there has been a rapidly growing interest in One Health approach to better understand and address the worldwide challenge of AR (Robinson *et al.* 2016).

For the improvement of the overall health of humans, animals and the environment, a concerted effort and cooperation among the three sectors is needed. However, previous studies have mainly been focused on AR in pathogenic bacteria in clinical settings or in wastewater, and AR bacteria and their AR genes in the environment are not well described. As aquatic environment is a hotspot for the development of AR bacteria, it is important to enhance our limited knowledge on the increasing AR of bacteria in the environment (Martinez 2009). Surface water receives pathogenic and non-pathogenic bacteria harbouring AR genes from human and animal wastes as well as antibiotic residues from healthcare, agricultural farms and industries that can serve as selective pressure. Aquatic environments can provide the opportunity for genetic materials, such as AR genes, to be exchanged between bacteria, and the transfer of AR genes to pathogenic bacteria is particularly a concern (Kenzaka *et al.* 2010; Walsh *et al.* 2011; Karkman *et al.* 2018). Such AR bacteria can then be transferred back to human population through exposure to contaminated water through drinking water, irrigation systems or recreational activities. To understand their impact on human health and food safety, AR bacteria in water and their environmental transmission routes to humans need to be assessed.

For this review article, *Salmonella*, *E. coli* and *Enterococcus* were chosen to evaluate the presence of primary pathogens and opportunistic pathogens in natural freshwaters. *Salmonella* has impact on human health as a pathogen, while *E. coli* and *Enterococcus* are not only indicators of faecal contamination of water but are also indicators of potential presence of pathogens. Moreover, *Salmonella*, *E. coli* and *Enterococcus* are commonly used as sentinel organisms for monitoring trends in resistance to antimicrobial agents with activity against Gram-negative as well as Gram-positive bacteria (WHO 2013). Since 1996, the National Antimicrobial Resistance Monitoring System (NARMS) has been monitoring the AR of selected bacteria, including *Salmonella*, *E. coli* and *Enterococcus*, isolated from humans, retail meats and food animals in the United States (U.S.FDA 2013a, 2013b). However, as a part of their One Health goal, NARMS may add an environmental component to their programme to monitor AR in surface water as well (personal communication). As such, a review of the presence of *Salmonella*, *E. coli* and *Enterococcus* in environmental water and their AR is warranted. AR in these three groups of bacteria are public health threats; extended spectrum beta (β) lactamase-producing Enterobacteriaceae (ESBL) and vancomycin-resistant *Enterococcus* (VRE) have been categorized as serious threats by the CDC while carbapenemase-resistant Enterobacteriaceae (CRE) has been categorized as an urgent threat (CDC 2019). This work serves to characterize populations of *Salmonella*, *E. coli* and *Enterococcus* present in the environmental water and their AR and fill the key data gap in understanding AR and minimizing its spread.

Salmonella

Salmonella as a pathogen

Salmonella is an enteric pathogen but is also ubiquitous and can be found in a wide variety of hosts including companion animals, farm animals and wild animals, as well as plants and insects (Brooks *et al.* 2001; Guo *et al.* 2002; Natvig *et al.* 2002; Holt *et al.* 2007; Dolejska *et al.* 2009; Mettee Zarecki *et al.* 2013; Bartholomew *et al.* 2014; Basler *et al.* 2016; Bosch *et al.* 2016). *Salmonella* has been traditionally considered as a foodborne bacteria that is transmitted through contaminated meat and animal products, but *Salmonella* infections through other transmission routes, such as contaminated fresh produce, contact with infected animals and contaminated water and soil, are commonly reported as well (Ailes *et al.* 2013; Jackson *et al.* 2013; Marus *et al.* 2019). *Salmonella* usually causes self-limiting gastroenteritis, and it is one of the leading causes of foodborne illnesses in developed countries; however, it can also be the etiological agent of invasive systemic diseases, for example, typhoid and paratyphoid fever which are rare in the United States but persistent in less developed countries (Lavigne and Blanc-Potard 2008; Levantesi *et al.* 2012; Chatham-Stephens *et al.* 2019). Most of *Salmonella* infections result in gastroenteritis that does not require antimicrobial treatments; however, antimicrobial therapy is required for the very young, the very old and immunocompromised patients who may develop extraintestinal infections, such as enteric fever, to prevent further complications (Varma *et al.* 2005). Infections caused by AR *Salmonella* limit treatment options and can be more severe than infections caused by

susceptible bacteria, increasing the rates of hospitalization, morbidity and mortality as well as the cost of treatment (Lee *et al.* 1994; Helms *et al.* 2002; Travers and Barza 2002; Varma *et al.* 2005; Foley and Lynne 2008). In the United States, 212 500 human infections associated with AR *Salmonella* are estimated with 70 deaths each year and the numbers are increasing (Lee *et al.* 1994; CDC 2018a; CDC 2019).

Salmonella in surface water

Life-threatening typhoid and paratyphoid fevers, caused by *Salmonella enterica* subsp. *enterica* serovar Typhi (*S.* Typhi) and *Salmonella enterica* subsp. *enterica* serovar Paratyphi (*S.* Paratyphi), respectively, still remain a major public health concern in developing countries, especially south-central and south-east Asia; and contamination of drinking water has been attributed as the main source of epidemic and endemic outbreaks (Crump *et al.* 2004; Bhan *et al.* 2005; Crump *et al.* 2015; Chatham-Stephens *et al.* 2019). While typhoidal *Salmonella* serotypes are involved in waterborne diseases in developing countries, non-typhoidal *Salmonella* (NTS) serotypes are mostly associated with animal products and increasingly with fresh produce in developed countries (Crump *et al.* 2015). *Salmonella* were traditionally considered zoonotic bacteria originating from animals; but recently, environments have been recognized as sources of *Salmonella*. Contaminated water and fresh produces irrigated with water contaminated with *Salmonella* from human and animal sources have been suggested to be sources of *Salmonella* infections (Schuster *et al.* 2005; Denno *et al.* 2009; Hanning *et al.* 2009; Clarkson *et al.* 2010; Craun *et al.* 2010; Dewey-Mattia *et al.* 2018). *Salmonella* were responsible for several waterborne outbreaks in the United States and Canada; source waters (e.g. groundwater and private wells), distribution systems (e.g. community water systems) and recreational water (e.g. fresh and salt waters) that had been contaminated by animal and human wastes were associated with these *Salmonella* waterborne outbreaks (Schuster *et al.* 2005; Denno *et al.* 2009; Clarkson *et al.* 2010; Craun *et al.* 2010). Furthermore, contaminated water has been indicated as the source of *Salmonella* outbreaks that involved fresh produce, including cucumbers, melons, tomatoes, lettuce, mangoes and sprouts (Hanning *et al.* 2009; Herman *et al.* 2015; Dewey-Mattia *et al.* 2018). In many cases, outbreak strains were isolated from waters used for irrigation and processing of the fresh fruits and vegetables (Hanning *et al.* 2009; Herman *et al.* 2015).

Recent studies show that *Salmonella* are frequently detected in surface water from different countries around the world (Lemarchand and Lebaron 2003; Meinersmann *et al.* 2008; Till *et al.* 2008; Jyoti *et al.* 2010; Schriewer *et al.* 2010; Jokinen *et al.* 2015). Their widespread occurrence in aquatic environments suggests that water may play a direct or indirect role in the transmission of *Salmonella* serving either as a vector or a reservoir for the bacteria. The potential contribution of surface water in *Salmonella* transmission to humans is a public health concern that needs to be addressed to reduce the burden of *Salmonella* infections in humans. Geographical and seasonal trends in *Salmonella* infections are apparent, such as increased cases of infections in the Southeastern states of the US and during summer months (CDC 2017, 2018b). Interestingly, studies conducted in the Southeastern US have shown that *Salmonella* are prevalent in surface water with significantly higher prevalence in summer (Haley *et al.* 2009; Li *et al.* 2014). The occurrence and persistence of *Salmonella* may be associated with seasonal changes in environmental conditions; for example, *Salmonella* detection levels in these watersheds have been shown to be correlated with both precipitation and temperature (Haley *et al.* 2009; Li *et al.* 2014). Seasonal and spatial patterns in the prevalence of *Salmonella* in the aquatic environment that coincide with the rate of cases of *Salmonella* infections supports the hypothesis that the environmental water plays a role in the transmission of human infections either directly as a vector or indirectly as a reservoir for *Salmonella*. However, the relationship between *Salmonella* occurrence in aquatic water and environmental factors is complex with numerous factors to consider. While studies in the Southeastern US suggested higher *Salmonella* prevalence in summer months in general, studies carried out in other parts of the world have shown varied seasonal peaks. The prevalence was highest during spring in Canada and during winter in New Zealand, Mexico and Czech Republic while others did not detect any significant seasonality (Simental and Martinez-Urtaza 2008; Till *et al.* 2008; Dolejska *et al.* 2009; Jokinen *et al.* 2010; Schriewer *et al.* 2010; Thomas *et al.* 2013). On the other hand, a positive correlation between precipitation and *Salmonella* detection rate is generally agreed upon (Simental and Martinez-Urtaza 2008; Haley *et al.* 2009; Jokinen *et al.* 2010; Luo *et al.* 2015). Rainfall is believed to transport bacteria from contamination sources into the water, increasing the bacterial load through runoff; however, Vereen *et al.* did not detect any *Salmonella* following a very heavy rainfall which suggests a dilution effect of the elevated precipitation on the stream water (Vereen *et al.* 2013). The same authors also reported no *Salmonella* detection during droughts reflecting no runoff from contaminated sources (Vereen *et al.* 2013). As such, predicting a seasonal pattern of *Salmonella* detection in environmental water is complicated as their occurrence may be influenced by seasonal differences in environmental parameters in different regions, including variable rainfall level and water temperature.

Salmonella were detected in diverse surface water sources of different landscapes with various detection rates ranging from below 10 to 100% (Lemarchand and Lebaron 2003; Till *et al.* 2008; Patchanee *et al.* 2010; Schriewer *et al.* 2010; Jokinen *et al.* 2015; Maurer *et al.* 2015). Several studies have shown that indicator organisms such as faecal coliform, *E. coli* and enterococci were not a good predictor of *Salmonella* presence in water as the concentrations of the indicator organisms did not associate with the detection rates of *Salmonella*, while Vereen *et al.* demonstrated that enterococci are a better indicator organism as elevated enterococci concentrations were significantly associated with higher *Salmonella* prevalence (Lemarchand and Lebaron 2003; Meinersmann *et al.* 2008; Till *et al.* 2008; Haley *et al.* 2009; Vereen *et al.* 2013; Luo *et al.* 2015). The prevalence of *Salmonella* increased at highly impacted water near the sources of pollution such as agricultural lands, farms and wastewater treatment plants, suggesting livestock and human sources of the contamination (Lemarchand and Lebaron 2003; Till *et al.* 2008; Jyoti *et al.* 2010; Vereen *et al.* 2013). Wildlife, including reptiles and birds, was also suggested to affect the *Salmonella* populations in the environment (Dolejska *et al.* 2009; Maurer *et al.* 2015). Reptile-associated *Salmonella* subsp. Arizonae was detected in up to 40·6% of the total *Salmonella* isolated by Haley *et al.* (2009), indicating a reptile origin of *Salmonella* in surface water. The same authors measured the concentrations of *Salmonella* in surface water which were positively correlated with water temperature and rainfall, with the highest concentrations observed in summer months, especially August (Haley *et al.* 2009). A high concentration of *Salmonella* was observed in highly contaminated rivers in India; 10^2–10^4 colony forming unit (CFU) per ml was observed in the rivers that receive untreated domestic wastewater (Jyoti *et al.* 2010). This measurement was higher by three to eight orders of magnitude compared to other studies carried out in developed countries, including the United States, France and New Zealand (Lemarchand and Lebaron 2003; Till *et al.* 2008; Haley *et al.* 2009; Luo *et al.* 2015). However, regardless of the landscapes, geographical location or sources of water, *Salmonella* were detected in all of the water environments under study, although there were variations in the detection rate and occurrence level. This suggests that aquatic environments are either a transient or permanent habitat for *Salmonella*, playing a role as a reservoir or vector for the bacteria to humans.

Diverse *Salmonella* serotypes were detected in aquatic environments with the total number of serotypes generally ranging from 10 to 43 (Catalao Dionisio *et al.* 2000; Meinersmann *et al.* 2008; Simental and Martinez-Urtaza 2008; Thomas *et al.* 2013; Jokinen *et al.* 2015; Luo *et al.* 2015; Maurer *et al.* 2015). Highest diversity of *Salmonella* serotypes was observed in the environment near the sources of pollution, such as animal farm that might contribute to the loading of *Salmonella* in surface water (Simental and Martinez-Urtaza 2008; Haley *et al.* 2009). Serotypes associated with human and animal infections were commonly recovered from surface water in the United States; however, the most common clinical serotypes such as *S. Enteritidis* and *S. Typhimurium* either were absent or constituted only a small fraction of the total *Salmonella* populations (Meinersmann *et al.* 2008; Haley *et al.* 2009; Patchanee *et al.* 2010; Li *et al.* 2014; McEgan *et al.* 2014; Maurer *et al.* 2015). Some of the most commonly identified serotypes in environmental waters were *S.* Braenderup, *S.* Hartford, *S.* Muenchen, *S.* Newport and *S.* Rubislaw, many of which are listed as common clinical serotypes, suggesting a link among *Salmonella* from humans, animals and the environment (Meinersmann *et al.* 2008; McEgan *et al.* 2014; Luo *et al.* 2015; Maurer *et al.* 2015). On the other hand, *S. Enteritidis* and *S. Typhimurium* formed a considerable portion of the *Salmonella* populations in countries outside the United States (Simental and Martinez-Urtaza 2008; Dolejska *et al.* 2009; Thomas *et al.* 2013; Jokinen *et al.* 2015). Streams in Mexico had a notably different *Salmonella* serotype distribution, identifying serotypes not recovered in other water environments, such as *S.* Vejle, *S.* Suberu and *S.* Othmarschen (Simental and Martinez-Urtaza 2008). This suggests that a regional difference in serotypes exists among *Salmonella* found in aquatic environments. A spatial trend in *Salmonella* serotype was emphasized by Jokinen *et al.* as they observed that certain serotypes were widespread throughout the watersheds while others were specific to particular regions, suggesting different sources of contamination (Jokinen *et al.* 2015).

More than 2 600 *Salmonella* serotypes have been identified so far; however, only a limited number of serotypes account for most of *Salmonella* infections in humans with *S. Typhimurium* and *S. Enteritidis* as the most common causes globally (Herikstad *et al.* 2002; Grimont and Weill 2007; Issenhuth-Jeanjean *et al.* 2014). Serotyping of *Salmonella* from surface water is important to identify any clinically important serotypes and to compare the composition of *Salmonella* serotypes in the environment with those in humans and animals, which will help evaluate the role of environmental water in the transmission of *Salmonella*. Serotypes often associated with humans and animals were frequently recovered from surface water, and this may indicate that a significant population of the bacteria move between human and water environment. Moreover, identification of serotypes that are specific to certain sources can help track the sources of *Salmonella* contamination. For example, Jokinen *et al.* frequently

recovered *S.* Kentucky, a serotype commonly associated with birds, from areas without intense poultry production (Jokinen *et al.* 2015). However, this was during months when birds actively migrate over these regions, allowing this information to suggest the potential source of *Salmonella* contamination as the migratory birds. Identification of *Salmonella* serotypes along with epidemiological data would help us fully understand the connection between water and humans and the directionality of the bacterial transmission.

A few studies were conducted in various parts of the world on the prevalence of AR *Salmonella* in surface water to understand the role of environmental water in the emergence and spread of AR in this genus. The results have shown that AR *Salmonella* are commonly detected in aquatic environments, including irrigation ponds, mixed-use watershed and rural rivers, thus increasing the risk of AR dissemination to humans (Meinersmann *et al.* 2008; Dolejska *et al.* 2009; Patchanee *et al.* 2010; Li *et al.* 2014; McEgan *et al.* 2014; Jokinen *et al.* 2015; Luo *et al.* 2015). In these studies, the detection rate of AR *Salmonella* varied from 10 to 99% with resistance to streptomycin observed in all of the water environments under study (Meinersmann *et al.* 2008; Dolejska *et al.* 2009; Patchanee *et al.* 2010; Li *et al.* 2014; McEgan *et al.* 2014; Jokinen *et al.* 2015; Luo *et al.* 2015). Interestingly, highest prevalence of AR *Salmonella* was observed in Florida while the lowest prevalence was detected in Georgia, both of which are the Southeastern states of the US (Meinersmann *et al.* 2008; McEgan *et al.* 2014; Luo *et al.* 2015). Patchanee *et al.* have shown that nearby pig farms were a potential source of AR *Salmonella* isolates recovered from the watersheds, whereas Dolejsk *et al.* suggested sea gulls as the source of AR *Salmonella* present in the water environment (Dolejska *et al.* 2009; Patchanee *et al.* 2010). Resistance to third-generation cephalosporin β-lactams including ceftriaxone, which is a recommended drug for salmonellosis, especially in children, was often detected in isolates from surface waters (Meinersmann *et al.* 2008; Patchanee *et al.* 2010; Li *et al.* 2014; Luo *et al.* 2015). Also concerning is the widespread presence of multidrug-resistant (MDR)-AmpC *S.* Newport in surface water of the irrigation ponds in Florida (Li *et al.* 2014). This particular strain of MDR *S.* Newport carrying an IncA/C plasmid with resistance to at least nine antimicrobials has contributed to the rapid and widespread emergence of MDR *S.* Newport among cattle and humans in the United States. This strain, identified as MDR-AmpC *S.* Newport, has caused the epidemic spread of the MDR phenotype to other *Salmonella* serotypes through the transfer of its IncA/C plasmid (CDC 2002; Frye and Jackson 2013). Pulse-field gel electrophoresis patterns of the MDR-AmpC *S.* Newport isolates from the irrigation ponds in Florida matched patterns in the CDC PulseNet database, indicating that these environmental isolates had also been recovered from human clinical samples (Li *et al.* 2014). These isolates present a high risk of spreading to humans since the water they were recovered from is used for the irrigation of produce. The presence of AR and MDR *Salmonella* in the environment not only is a public health concern but also suggests an extensive contamination from nearby animal farms or residential areas.

Resistance to β-lactams is particularly a concern in *Salmonella* as fluoroquinolones are not approved for children and pregnant women due to concerns about fluoroquinolones interfering with cartilage formation (Parry and Threlfall 2008). β-lactamases mediate resistance to β-lactams, and the main β-lactamases involved in resistance to extended-spectrum cephalosporins are AmpC β-lactamases, extended spectrum β-lactamases (ESBLs) and carbapenemases (Poole 2004). In *Salmonella*, the most prevalent β-lactamase resistance mechanism is plasmid-encoded AmpC β-lactamases, while ESBLs are comparatively rare in the United States (Winokur *et al.* 2000; Zhao *et al.* 2003; Folster *et al.* 2010; Sjölund-Karlsson *et al.* 2010). Among the AmpC plasmid-mediated β-lactamases, cephamycinases (CMY) encoded by bla_{CMY} genes are predominant, out of which $bla_{\text{CMY-2}}$ is most prevalent and widely spread (Philippon *et al.* 2002). However, while $bla_{\text{CMY-2}}$ is widespread among humans and animals, the prevalence of this gene in environmental water is not well described. Wei *et al.* and Agga *et al.* attempted to identify $bla_{\text{CMY-2}}$ in their isolates recovered from environmental water in China using PCR and in the United States using microarray, respectively, but none of their environmental isolates carried the gene (Agga *et al.* 2015; Wei *et al.* 2019). Zheng *et al.* and Arai *et al.* sequenced the whole genomes of a few selected *Salmonella* isolates from environmental water, but none of their isolates contained AmpC β-lactamase or ESBL genes (Zheng *et al.* 2017; Arai *et al.* 2018).

While studies on the phenotypic characterization of AR environmental *Salmonella* isolates are occasionally presented, the genotypic characterization of isolates from aquatic environments to investigate their AR genes and associated MGEs involved in horizontal gene transfer are lacking. Comprehensive studies that involve sequence analyses of environmental AR isolates are needed to enhance our understanding of the genetic contents of the isolates, the mechanisms of their AR gene transfer and the potential for AR gene transmission in the environment. Analysis of the resistance mechanisms can also be used to determine the genetic relationship between resistances found in isolates from environmental water and humans. Because of the diversity of genetic elements that leads to AR, it may be possible to determine whether

resistances seen in bacterial isolates from the environment are closely related to those found in human infections and animal isolates. Similarity between isolates may indicate that environmental water is a direct vector for human infections or a reservoir that harbours bacteria which could develop resistance and then reach humans by some intermediates, such as food animals.

Escherichia coli

Commensal and pathogenic E. coli

Escherichia coli is a commensal bacteria residing in the gastrointestinal tract of warm-blooded animals including humans without causing diseases except in immunocompromised hosts or when the gastrointestinal barriers are breached (Nataro and Kaper 1998; Kaper *et al.* 2004; Croxen *et al.* 2013). However, certain *E. coli* acquired virulence factors encoded on mobile genetic elements, such as bacteriophages, pathogenicity islands, plasmids and transposons, through horizontal gene transfer becoming pathogenic and causing diarrheal and extraintestinal diseases (Nataro and Kaper 1998; Kaper *et al.* 2004; Croxen *et al.* 2013). While extraintestinal pathogenic *E. coli* (ExPEC) causes infections outside of the gastrointestinal tract, such as urinary tract infections, sepsis and neonatal meningitis, diarrheagenic *E. coli* cause diarrhoea and other gastrointestinal diseases (Nataro and Kaper 1998; Kohler and Dobrindt 2011). Most well-described diarrheagenic *E. coli* pathotypes, based on their pathogenesis mechanisms and virulence factors, are enteroaggregative *E. coli* (EAEC), enteroinvasive *E. coli* (EIEC), enteropathogenic *E. coli* (EPEC), enterotoxigenic *E. coli* (ETEC), enterohaemorrhagic *E. coli* (EHEC) and diffusely adherent *E. coli* (DAEC) (Kaper *et al.* 2004). Together, these pathogenic *E. coli* strains are a significant cause of global morbidity and mortality (Nataro and Kaper 1998; Kaper *et al.* 2004; Croxen *et al.* 2013). Such pathogenic *E. coli* were responsible for sporadic cases and outbreaks associated with contaminated recreational and drinking water. Recreational water-associated outbreaks occurred in lakes, rivers, ponds, streams and swimming pools (Keene *et al.* 1994; McCarthy *et al.* 2001; Craun *et al.* 2005; Verma *et al.* 2007; Probert *et al.* 2017). Drinking water-associated outbreaks were attributed to well water, municipal water and spring water (Rosenberg *et al.* 1977; Charatan 1999; Olsen *et al.* 2002; Hrudey *et al.* 2003; Craun *et al.* 2010). The outbreak that occurred in Walkerton, Canada in 2000 was the largest outbreak reported associated with drinking water, affecting more than 2,300 individuals with seven deaths (Hrudey *et al.* 2003). The frequent occurrence of waterborne outbreaks shows that contaminated water is an effective transmission vehicle of *E. coli*. Pathogenic *E. coli* that are resistant to therapeutic antimicrobials have increased during the last decades; *E. coli* resistant to first-line antimicrobial agents, including extended-spectrum cephalosporins and fluoroquinolones, are of particular concern as they complicate effective treatments for *E. coli* infections (WHO 2014). These AR *E. coli* are one of the nine bacteria of international concern according to the WHO report as they are one of the most common causes of infections in the community as well as in hospital settings worldwide (WHO 2014).

E. coli in surface water

Environmental water sources are prone to contamination by *E. coli* from both humans and other warm-blooded animals. Possible human sources include discharge of wastewater, sewage leaks, and failing septic tanks and drain fields. Additionally, partially treated sewage is sometimes directly discharged into rivers, intentionally or unintentionally, often enhanced by storm events that have been shown to increase *E. coli* counts in water by several folds (Sidhu *et al.* 2012; Sidhu *et al.* 2013; Cho *et al.* 2018). Animal sources include runoffs from livestock farms, land application of animal waste, pet wastes from parks, and wildlife such as geese, raccoons and deer (Fairbrother and Nadeau 2006; Somarelli *et al.* 2007). *E. coli* are ubiquitous in human faeces and the environment; thus, they are used as an indicator of faecal contamination for assessing water quality (U.S.EPA 2012). They are not generally considered pathogens, but their presence indicates potential presence of pathogens as high *E. coli* levels in recreational waters have been shown to be associated with an increased risk of swimming-associated gastrointestinal illness (Dufour 1984; Wade *et al.* 2003). In addition, simple and unsophisticated methods to culture, detect and enumerate *E. coli* make them a good indicator organism. *E. coli*, along with enterococci, replaced faecal coliforms as an indicator of faecal contamination by EPA in 1986 as they were a better predictor of gastrointestinal illness in recreational water (U.S.EPA 1986). In the United States, EPA standards for *E. coli* are either 126 *E. coli* CFU per 100 ml of water or less based on a geometric mean or a single-sample measurement not greater than 235 CFU per 100 ml in freshwater for the purpose of primary contact recreation such as swimming, surfing, tubing and water skiing, which involves full-body contact with water (U.S.EPA 1986).

On the other hand, the use of *E. coli* as an indicator of faecal contamination has been put into question as 'naturalized' *E. coli* have been shown to persist in water environments regardless of the faecal input into the environment (Rivera *et al.* 1988; Power *et al.* 2005). Despite the adverse environmental conditions, such as UV radiation, temperature fluctuation, predation and limited nutrients, *E. coli* are present in the environment

in a large number outside their primary habitat within the host; half of the entire *E. coli* population are estimated to be outside of the host in this secondary habitat (Savageau 1983). Further studies suggested that a specialized subset of *E. coli* strains can survive and grow in the environment, and a considerable population of these environmentally adapted, or 'naturalized' *E. coli*, which is distinct from faecal *E. coli*, can be found in various environments, such as water, soil and sediment (Gordon *et al.* 2002; Byappanahalli *et al.* 2003; Ishii *et al.* 2006; Ishii *et al.* 2007; Walk *et al.* 2007). Walk *et al.* characterized *E. coli* isolates from the aquatic environment using multilocus sequence typing (MLST) and identified environmentally adapted lineages of *E. coli*: ET-1 clade, which is a subset of the B1 phylogenetic group, and cryptic clades CIII, CIV and CV (Walk *et al.* 2007; Walk *et al.* 2009). The authors also suggested that approximately one-fourth of their environmental *E. coli* from freshwater beaches was strains adapted to the environment (Walk *et al.* 2007). Out of the four major phylogenetic groups of *E. coli*, referred to as A, B1, B2, and D, B2 and D groups are associated with extraintestinal infections, and members of A and B1 groups are generally commensal *E. coli* (Picard *et al.* 1999). B1 group was the most commonly identified group in the freshwater beach study by Walk *et al.*, supporting the recent finding that B1 strains are host generalists and environmentally adaptive, in contrast to B2 strains, which are more host-adapted (Walk *et al.* 2007; White *et al.* 2011; Meric *et al.* 2013). In their study, Gordon *et al.* (2002) compared *E. coli* isolated from septic tanks with those isolated from the people using the septic tanks and found out that the strains from the septic tanks were distinct from the human strains and adapted better to the conditions of the external environment. These results underscore the presence of 'naturalized' *E. coli* populations that persist better outside of the host in their secondary habitat.

Few studies have determined the presence of virulence genes in *E. coli* isolated from environmental water to examine the frequency of potential pathogenic *E. coli* (Lauber *et al.* 2003; Hamelin *et al.* 2006; Hamelin *et al.* 2007; Ishii *et al.* 2007; Ram *et al.* 2008; Sidhu *et al.* 2013; Titilawo *et al.* 2015b; Cho *et al.* 2018; Haymaker *et al.* 2019). Some of the most commonly detected *E. coli* pathotypes include ETEC, defined by the ability to produce heat-labile (LT) and/or heat-stable (ST) enterotoxins and causes traveller's diarrhoea; EPEC, defined by the ability to produce intimin adhesin protein and causes infant diarrhoea; and EHEC, defined by the ability to produce Shiga toxin and intimin and are the causative agent of haemorrhagic colitis and haemolytic uremic syndrome (Nataro and Kaper 1998). Virulence genes were detected with varying frequency in different environmental water around the world. Virulence genes were detected in 91, 61·1 and 85% of the isolates from rivers and creeks in Nigeria, India and Australia, respectively (Ram *et al.* 2008; Sidhu *et al.* 2013; Titilawo *et al.* 2015b). On the other hand, virulence genes were detected at a much lower rate, sometimes less than 1%, in the studies by Lauber *et al.* (2003), Ishii *et al.* (2007), Cho *et al.* (2018), Haymaker *et al.* (2019), all of which were conducted in surface waters of the United States. One of the most common virulence genes found in these studies was *eaeA*, a gene that encodes intimin protein in EPEC and EHEC; however, while EPEC was frequently isolated from surface water sources, EHEC, which carry additional Shiga toxin genes, *stx1*, *stx2* or both, was not often detected (Lauber *et al.* 2003; Ishii *et al.* 2007; Titilawo *et al.* 2015b; Cho *et al.* 2018; Haymaker *et al.* 2019). Only Ram *et al.* detected more EHEC strains than EPEC strains in the Gomti River, which is one of the most polluted rivers in India, and Sidhu *et al.* detected EHEC as often as EPEC in Australia, while the former study detected more *stx1* and the latter study detected more *stx2* genes (Ram *et al.* 2008; Sidhu *et al.* 2013). EHEC with Shiga toxin type 2 (Stx2) are more commonly associated with severe complications than those producing Shiga toxin type 1 (Stx1) (Paton and Paton 1998). Shiga-toxin producing *E. coli* (STEC), of which EHEC is a subset, produces Shiga toxin but not intimin protein (Nataro and Kaper 1998). Even though not all STEC strains are considered pathogens, STEC were frequently detected from surface waters as well (Ram *et al.* 2008; Sidhu *et al.* 2013; Titilawo *et al.* 2015b; Cho *et al.* 2018; Haymaker *et al.* 2019). ETEC was detected in surface waters of Australia, India and Nigeria at 5·7, 21·1 and 45% detection rates, respectively, while no ETEC was detected in US waters (Lauber *et al.* 2003; Ram *et al.* 2008; Sidhu *et al.* 2013; Titilawo *et al.* 2015b; Cho *et al.* 2018). As such, a variety of pathotypes seems to be present at higher frequency rates in countries other than the United States. Additionally, it should be noted that many of the chromogenic media used for the isolation of *E. coli* are based on their presence of β-glucuronidase enzyme; however, EHEC, such as O157:H7 strain, lacks β-glucuronidase and as such, the prevalence of EHEC in water is likely underestimated relative to other pathotypes of *E. coli* (Ratnam *et al.* 1988; Maheux *et al.* 2015).

While most studies focused on diarrheagenic or intestinal *E. coli*, Hamelin *et al.* included ExPEC in their two studies carried out in Canada and found that a higher percentage of ExPEC was present than the diarrheagenic *E. coli* strains in environmental waters (Hamelin *et al.* 2006; Hamelin *et al.* 2007). Approximately 28% and 26% of the total isolates belonged to ExPEC, including neonatal meningitis-associated *E. coli* (MNEC), uropathogenic

E. coli (UPEC) and septicaemia-associated *E. coli* (SEPEC), while only 4 and 2% belonged to diarrheagenic pathotypes in their studies covering St. Clair River and Detroit River areas and Lake Ontario, respectively (Hamelin *et al.* 2006; Hamelin *et al.* 2007). Nevertheless, it is difficult to make direct comparisons between the results from different studies due to differences in methodology for isolation and detection of pathogenic *E. coli* (enrichment *vs* non-enrichment, PCR *vs* microarray) and the choice of virulence genes screened. Although the detection of virulence genes does not indicate the pathogenic potential of the *E. coli* isolates, and phenotypic tests need to be performed to establish the ability of these *E. coli* to cause diseases, the widespread distribution of virulence genes and potential pathogenic *E. coli* in streams and rivers used for recreations, consumption and irrigation raises human health risks with exposure to these water sources.

Storm events not only increase the number of *E. coli* and increase the number of *E. coli* with multiple virulence genes in environmental waters but also evenly distribute the prevalence of *E. coli* pathotypes in surface water bodies by significantly lowering the number of certain pathotypes and increasing the number of other pathotypes (Sidhu *et al.* 2013). This uniform distribution of pathotypes after rainfall was suggested to be due to the transport of pathogenic *E. coli* into the water from both point sources (single identifiable sources) and nonpoint sources (many diffuse sources) (Sidhu *et al.* 2013). Rain also increases the number of STEC of serotype O157:H7 by disseminating bacteria from point sources, such as animal faeces, especially cattle, which are a known reservoir of STEC, or by release of bacteria from sediments (Hussein and Sakuma 2005; Cooley *et al.* 2007). Of all the pathotypes of *E. coli* that are associated with human infections, the O157:H7 strain is the most well-known pathogenic strain, responsible for the majority of *E. coli* outbreaks reported and mortality worldwide (Nataro and Kaper 1998; CDC 2016). Studies showed that the *E. coli* O157:H7 and other strains belonging to the serogroup O157 were present in environmental waters, and the presence of these pathogenic *E. coli* in surface water highlights the potential risk to human health through consumption of untreated water and irrigated raw vegetables, as well as through recreational use of surface water (Cooley *et al.* 2007; Jokinen *et al.* 2010; Maal-Bared *et al.* 2013; Cooley *et al.* 2014). In fact, the *E. coli* O157:H7 outbreak in Walkerton, Ontario, Canada in 2000, which caused 2 300 cases of gastrointestinal illness and seven deaths, was attributed to the contamination of well water with cattle manure from a nearby farm following intense rainfall events (Hrudey *et al.* 2003; Auld *et al.* 2004). The presence of *E. coli* O157 in water sources near agricultural lands including cattle farms suggests the animal source of the pathogens (Cooley *et al.* 2007; Maal-Bared *et al.* 2013; Cooley *et al.* 2014). As such, wildlife and livestock that have direct, uncontrolled access to surface waters may be the source of the pathogens, while heavy rainfall are the means whereby pathogens in animal manure may be transported to surface waters.

The prevalence of AR *E. coli* in environmental water has been shown to vary from <10 to 100%, and these variations may be due to differences in the use and regulations of antimicrobials among countries or differences in the source of faecal contamination impacting the water sources (Servais and Passerat 2009; Agga *et al.* 2015; Titilawo *et al.* 2015a; Lyimo *et al.* 2016; Chen *et al.* 2017; Cho *et al.* 2018). However, a direct comparison between these studies is difficult as different antimicrobial drugs were used to assess the antimicrobial susceptibility of environmental *E. coli*. Nevertheless, resistances to sulphonamides (sulfamethoxazole, trimethoprim/sulfamethoxazole), β-lactams (penicillin, ampicillin and amoxicillin) and tetracycline were generally widespread (Servais and Passerat 2009; Agga *et al.* 2015; Titilawo *et al.* 2015a; Lyimo *et al.* 2016; Chen *et al.* 2017; Cho *et al.* 2018). Resistance to third-generation cephalosporins, which are used to treat *E. coli* infections, was often observed as well from the *E. coli* isolates recovered from surface waters (Pitout 2012; Blaak *et al.* 2014; Agga *et al.* 2015; Bajaj *et al.* 2015; Jorgensen *et al.* 2017; Cho *et al.* 2018). Wastewater released into the waterways were implicated to be the main source of AR bacteria, but the presence of AR *E. coli* in streams with low or no obvious contamination level suggests that either wildlife and companion animals or runoffs from surrounding lands and sediments enhanced by rainfall contribute to the AR *E. coli* contamination in waters (Servais and Passerat 2009; Agga *et al.* 2015; McArthur *et al.* 2016).

ESBL-producing *E. coli* were identified not only from recreational water but also from wastewater treatment plant effluents and receiving surface water at a high detection rate (Blaak *et al.* 2014; Agga *et al.* 2015; Titilawo *et al.* 2015a; Kittinger *et al.* 2016; Lyimo *et al.* 2016; Jorgensen *et al.* 2017). In *E. coli*, resistance to expanded-spectrum cephalosporins is usually due to ESBLs, which destroy β-lactam antimicrobial drugs (Vila *et al.* 2016). Of all the ESBL genes, $bla_{\text{CTX-M}}$, particularly $bla_{\text{CTX-M-15}}$, and bla_{TEM}, particularly $bla_{\text{TEM-1}}$, were often detected in surface water with bla_{SHV} and bla_{OXA} occasionally identified (Cho *et al.* in press; Blaak *et al.* 2014; Agga *et al.* 2015; Titilawo *et al.* 2015a; Kittinger *et al.* 2016; Lyimo *et al.* 2016; Jorgensen *et al.* 2017; Cho *et al.* 2019a). This observation reflects the current trend of CTX-M (cefotaximase-Munich) enzymes as the dominant type of enzymes among ESBL-producing *E. coli*, of which CTX-M-15 is most widely distributed in community and hospitals

(Canton and Coque 2006; Coque *et al.* 2008). *Escherichia coli* ST131, which is a pandemic *E. coli* strain that can be MDR, and is globally disseminated causing hospital and community-acquired infections around the world, were also prevalent in surface water (Nicolas-Chanoine *et al.* 2008; Johnson *et al.* 2010; Hu *et al.* 2013; Nicolas-Chanoine *et al.* 2014; Petty *et al.* 2014; Assawatheptawee *et al.* 2017; Jorgensen *et al.* 2017; Runcharoen *et al.* 2017; Cho *et al.* 2018).

Carbapenem-resistant Enterobacteriaceae (CRE) have increased recently, and the CDC has recognized them as an urgent public health threat as these bacteria are resistant to nearly all of the available antimicrobial drugs and the mortality rate of the CRE infections is high (CDC 2013; Thaden *et al.* 2014). CRE have been frequently detected beyond human healthcare in water environments around the world. Researchers have detected carbapenemase-producing *Enterobacteriaceae*, such as *Enterobacter* sp., *Klebsiella* sp. and *Kluyvera* sp., and various concentrations of carbapenemase genes, such as bla_{KPC}, bla_{NDM} and bla_{OXA-48}, in surface waters (Ahammad *et al.* 2014; Montezzi *et al.* 2015; Proia *et al.* 2018; Mathys *et al.* 2019). Carbapenemase-producing *E. coli* have been identified in surface waters from different countries, including China, Ireland, Lebanon, Portugal and the United States, especially downstream of wastewater treatment plants (Poirel *et al.* 2012; Xu *et al.* 2015; Kieffer *et al.* 2016; Mahon *et al.* 2017; Yang *et al.* 2017; Diab *et al.* 2018; Mathys *et al.* 2019). The detection of CRE in both effluents and receiving waters suggests that CRE dissemination into the environment occurs through wastewater. Furthermore, the presence of *mcr-1*, which encodes resistance to colistin, a drug of last resort, in environmental waters, though at a very low rate, is daunting (Nation and Li 2009; Schwarz and Johnson 2016; Yu *et al.* 2016; Zurfuh *et al.* 2016; Jorgensen *et al.* 2017; Runcharoen *et al.* 2017). Colistin has been in use since 1950s but, due to its toxicity, the drug has not been in use until recently when MDR became a worldwide problem, which has resulted in colistin being considered the drug of last resort (Lim *et al.* 2010). Colistin resistance was chromosomally encoded and was not of a concern; therefore, when plasmid-mediated *mcr-1* gene was described for the first time in *E. coli* by Liu *et al.* (2016), many scientists underwent a retrospective screening of their old *E. coli* isolates for *mcr-1* gene detection and *mcr-1*-carrying isolates were reported as early as in the 1980s (Liu *et al.* 2016; Shen *et al.* 2016). The identification of *mcr-1* gene from a Malaysian pond water in a retrospective study by Yu *et al.* and from recent studies by Jorgensen *et al.* and Runcharoen *et al.* in Norway and Thailand, respectively, suggests the potential widespread distribution of colistin-resistant *E. coli* in the environment, which may not be a recent emergence or on a rising trend (Yu *et al.* 2016; Jorgensen *et al.* 2017; Runcharoen *et al.* 2017).

Enterococcus

Commensal and pathogenic Enterococcus

Enterococci are Gram-positive bacteria that naturally reside in intestinal tracts of humans and animals including mammals, insects, reptiles and birds (Mundt 1963b; Martin and Mundt 1972). They are also found in the environments including water, soil and plants due to their high tolerance to different conditions (Mundt 1963a; Fujioka *et al.* 1999; Badgley *et al.* 2010). They can survive in a wide range of temperatures (5–60°C) and pH (4·6–9·9), in the presence of high salt concentration (6·5% NaCl) and bile salts (40%), and in prolonged desiccation (Fisher and Phillips 2009). Enterococci have been a major nosocomial pathogen since the 1970s and has been considered the fifth most common healthcare-associated pathogen in the United States in 2015 (Jett *et al.* 1994; Magill *et al.* 2018). Of the 58 enterococcal species identified, *E. faecalis* and *E. faecium*, which are also most common enterococcal species in the intestinal microbiota of humans, account for most of the enterococcal infections in humans (Tannock and Cook 2002; Parte 2018). Other species, including *E. avium*, *E. casseliflauvus*, *E. durans*, *E. gallinarum*, *E. hirae*, *E. mundtii* and *E. raffinosus*, are also responsible for human infections (Tannock and Cook 2002). Enterococci have become a major nosocomial pathogen due to their resistance to several antimicrobials and ability to acquire and disseminate AR determinants. They are intrinsically resistant to a broad range of antimicrobials such as β-lactams and aminoglycosides (Arias and Murray 2012). Furthermore, they have acquired resistance to almost all currently used and new clinical antimicrobial drugs, further complicating antimicrobial treatments (Arias and Murray 2012). However, it was not until the acquisition of vancomycin resistance that enterococci have drawn attention as an MDR pathogen. Vancomycin-resistant *Enterococcus* (VRE) is considered a serious threat level by the CDC as only a few antimicrobial options are available for the treatment of VRE infections (CDC 2019). Linezolid, quinupristin/dalfopristin, daptomycin and tigecycline are used for the treatment of VRE infections; but unfortunately, resistance to these drugs is increasingly reported making the VRE infections difficult to treat (Arias and Murray 2012; Rossolini *et al.* 2014; Guzman Prieto *et al.* 2016; Cho *et al.* 2019b).

Enterococcus in surface water

Along with *E. coli*, enterococci are used as an indicator of faecal contamination in freshwater, and in marine water, enterococci are considered a better indicator of faecal

pollution than *E. coli* as their concentrations in the marine water are positively associated with swimming-associated gastrointestinal illness rates (Cabelli 1983; Dufour 1984). U.S. EPA recommends no more than either a geometric mean of 33 *Enterococcus* CFU per 100 ml of water or a single-sample measurement of 61 CFU per 100 ml for freshwater, and either a geometric mean of 35 *Enterococcus* CFU per 100 ml or a single-sample measurement of 104 CFU per 100 ml for marine water as the water quality criteria for primary contact recreational activities with a high probability of water ingestion, such as swimming, diving, surfing and bathing (U.S.EPA 1986).

Certain species of *Enterococcus*, such as *E. faecalis*, *E. faecium*, *E. casseliflavus*, *E. gallinarum*, *E. mundtii*, *E. hirae*, *E. durans* and *E. avium*, are consistently recovered from surface water around the world, although in different proportions. Research has shown that *E. faecalis* is usually the most common species in this niche (Lata *et al.* 2009; Alipour *et al.* 2014; Sidhu *et al.* 2014; Molale and Bezuidenhout 2016). In fact, *E. faecalis* has a broad host range and is the most widely distributed enterococcal species as it has been isolated from humans (hospital and community settings), animals (livestock, companion animals and wild animals) and the environment (Guzman Prieto *et al.* 2016). While *E. faecalis* appears to be the most abundant species in natural water in a majority of studies, other species such as *E. faecium*, *E. casseliflavus*, *E. hirae* and *E. mundtii* were found to be dominant or as frequent as *E. faecalis* in some water environments (Svec and Sedlácek 1999; Meinersmann *et al.* 2008; Ran *et al.* 2013; Molale and Bezuidenhout 2016; Cho *et al.* 2019b).

This difference in species compositions at different locations could be due to spatial or temporal variability. Environmental factors were suggested to influence the species compositions, with warm temperature favouring the bacterial growth and rainfall transporting bacteria into water along with runoff from surrounding vegetation and soil, animal faecal matter, sewage leakage and anthropogenic activities (Ran *et al.* 2013; Sidhu *et al.* 2014). Ran *et al.* reported an increase in the frequency of *E. faecalis* during summer months and after rainfall events potentially due to runoff transporting more of the faecal origin species, while Sidhu *et al.* reported a decrease in the frequency of *E. faecalis* after rainfall events possibly due to other species of *Enterococcus* being added into the waterbodies from various contamination sources, thus decreasing the proportion of *E. faecalis* of all *Enterococcus* species isolated (Ran *et al.* 2013; Sidhu *et al.* 2014). On the other hand, Kühn (2003) reported a spatial variability in the species composition as surface water receiving rural runoff contained almost no *E. faecalis* and exhibited a similar species distribution to the surrounding farmland.

There has been a debate on the identification of potential contamination source based on the presence of specific *Enterococcus* species associated with the source. Presence of soil and plant origin *E. casseliflavus* and *E. mundtii* suggests plants and soil as a source of enterococci, while the presence of faecal origin *E. faecalis* and *E. faecium* suggests human and animal as a source of enterococci in water, increasing the potential health risk due to pathogens originating from humans and animals. Sidhu *et al.* (2014) found that *E. faecalis* was more prevalent in creeks within high urbanization landscape with more human and animal faecal input, and *E. casseliflavus* and *E. mundtii* being more prevalent in creeks with low urbanization and high vegetation. Ferguson *et al.* (2013) also reported a similar finding with a higher proportion of *E. casseliflavus* and *E. mundtii* in beach and surface water samples compared to wastewater samples that were dominated by *E. faecalis* and *E. faecium*. Alternatively, some studies were sceptical of the use of a host-specific species as an indicator of either human faecal contamination or environmental residues as similar patterns of *Enterococcus* species composition were seen from various hosts (Layton *et al.* 2010; Lebreton *et al.* 2014). A number of *Enterococcus* species have been isolated from human faeces, animal faeces, environment and food, so it is a challenging task to identify a single host for each species found in the environmental water.

Different cultivation methods used for the recovery of *Enterococcus* isolates could contribute towards the variability in species composition found in different water studies. The nature of culture media, either solid or liquid, and the composition of media with different substrates, selective agents and indicator molecules were suggested to affect species populations recovered (Jackson *et al.* 2005; Ferguson *et al.* 2013). In addition, culture conditions may account for species variability. As different enterococcal species have different physical properties and growth characteristics, a change in incubation temperature had an effect on the recovery and selection of certain species (Domig *et al.* 2003; Jackson *et al.* 2005). According to the study conducted by Jackson *et al.* (2005), *E. faecalis*, *E. casseliflavus* and *E. durans* were more temperature sensitive than *E. faecium* and *E. hirae*, as more isolates were recovered at 37°C than at higher temperatures of 42 or 45°C.

Not only does isolation method affect the species composition but so does the species identification method. Enterococcal species identification has been based on either phenotypic methods, such as conventional morphological and biochemical tests and VITEK, or genotypic methods, such as 16S rRNA gene sequencing and multiplex PCR (Patel *et al.* 1998; Jackson *et al.* 2004). Discrepancy in species identification occurs between different

methods, either overestimating or underestimating certain species (Patel *et al.* 1998; Fang *et al.* 2012; Ferguson *et al.* 2013). A simple standardized method to identify enterococci to the species level is required to enable direct comparisons of species distribution; however, methodology is beyond the scope of this review. More recently, novel *Enterococcus* species have been identified from various water samples including *E. rivorum*, *E. haemoperoxidus*, *E. moraviensis*, *E. aquimarinus*, *E. silesiacus*, *E. ureasiticus*, *E. quebecensis*, *E. ureilyticus* and *E. rotai* (Svec *et al.* 2001; Svec *et al.* 2005; Svec *et al.* 2006; Niemi *et al.* 2012; Sistek *et al.* 2012; Sedlacek *et al.* 2013). Since the list of *Enterococcus* species is expanding as their habitats are explored, and as enterococci are isolated from diverse sample types owing to their ubiquity, a consistent and reliable standardized method to isolate enterococci and identify their species is needed, especially if the species identification could point us to the contamination source.

Several studies have demonstrated that enterococci in environmental water are resistant to a wide range of antimicrobials, the results of which indicate that AR enterococci are not limited to the clinical settings and are prevalent and persistent in the environment (Rice *et al.* 1995; Meinersmann *et al.* 2008; Moore *et al.* 2008; Lata *et al.* 2009; Cho *et al.* 2019b). Surface waters receive AR enterococci from hospitals and other sources through discharged sewage or other means, increasing the prevalence of these bacteria in the environment and thus increasing the risk to human health through drinking and recreational activities. Even though VRE are not frequently isolated from uncontaminated aquatic environments, discharged sewage can release VRE from hospitals into aquatic environments (Harwood *et al.* 2001; Moore *et al.* 2008; Young *et al.* 2016). Although not frequently, VRE have been detected in aquatic environments, outgoing treated sewage and receiving surface water around the world (Iversen *et al.* 2002; Novais *et al.* 2005; Lata *et al.* 2009; Rosenberg Goldstein *et al.* 2014; Young *et al.* 2016). Their origin has been suggested to be surrounding hospitals and community as healthy individuals have also been shown to carry VRE, and drugs released into surface water may sustain VRE in the environment (Wendt *et al.* 1999; Padiglione *et al.* 2000; Novais *et al.* 2005). Iversen *et al.* (2002) demonstrated in their study in Sweden that VRE were only detected in sewage from the hospital that had used 10 times as much vancomycin as the other hospital from where no VRE was identified, suggesting that the amount of the drug used in the hospitals may influence the prevalence of VRE.

The prevalence of VRE in the United States outside the clinical setting is lower than in other countries, and no VRE have been detected in US surface water without the obvious contamination after a spill of sewage (Harwood *et al.* 2001; Young *et al.* 2016). On the other hand, VRE have been detected in surface water in several European countries (Iversen *et al.* 2002; Blanch *et al.* 2003; Novais *et al.* 2005). This could be because avoparcin, which belongs to the same glycopeptide antimicrobial class as vancomycin, was never allowed in animals as growth promoter in the United States, while in some European countries, it was used at sub-therapeutic doses as a growth promoter in animal farms, providing selective pressure for vancomycin resistance in enterococci among livestock (Bager *et al.* 1997; McDonald *et al.* 1997; Kruse *et al.* 1999). Concerns regarding the cross-resistance between avoparcin and vancomycin and the farm animals as a reservoir of VRE have led to the ban of avoparcin in the entire European Union from 1997, and decreased prevalence of VRE was reported among animals and healthy humans in the community following the discontinued use of the drug (Bager *et al.* 1999; Klare *et al.* 1999).

E. casseliflavus and *E. gallinarum* with reduced susceptibility to vancomycin carrying *vanC* were often detected in environmental waters (Nam *et al.* 2013; Nishiyama *et al.* 2015). *E. casseliflavus* and *E. gallinarum* are intrinsically resistant to vancomycin but have attracted less attention compared to vancomycin-resistant *E. faecalis* and *E. faecium* for several reasons (Clark *et al.* 1998). First of all, *E. casseliflavus* and *E. gallinarum* are considered to be 'environmental' species that are primarily associated with plants and birds (Mundt and Graham 1968; Collins *et al.* 1984). They are not considered clinically significant pathogens as these two enterococcal species cause human infections less frequently compared to *E. faecalis* and *E. faecium* (Toye *et al.* 1997). Also, MIC of *E. casseliflavus* and *E. gallinarum* for vancomycin is not usually higher than the CLSI breakpoint of 32 μg ml^{-1}, making the treatments of infections due to these bacteria relatively less challenging (Gold 2001). In addition, *vanC* gene, which encodes intrinsic resistance to vancomycin in *E. casseliflavus* and *E. gallinarum*, is chromosomally encoded and not transferable (Gold 2001). However, the clinical significance of *vanC*-carrying species should not be overlooked. Although not frequently, global incidence of infections due to VanC-type *E. casseliflavus* and *E. gallinarum* has been identified, for which vancomycin therapy failed in some cases (Green *et al.* 1991; Reid *et al.* 2001; Choi *et al.* 2004; de Perio *et al.* 2006; Contreras *et al.* 2008; Cooper *et al.* 2008). Furthermore, *E. casseliflavus* and *E. gallinarum* exhibiting high-level vancomycin resistance phenotype have been detected in clinical isolates with the acquisition of *vanA* and *vanB* genes which are transferable to other enterococci (Dutka-Malen *et al.* 1994; Liassine *et al.* 1998; Corso *et al.* 2005; Merquior *et al.* 2008). The increasing cases of infections

and outbreaks of these less common enterococci suggests a need for increased clinical attention.

Due to their ubiquity in the animal gut, resilience to environmental stress, resistance to clinically important antimicrobials and ability to acquire and transfer resistance, enterococci are used as sentinel organisms for AR with activity against Gram-positive bacteria, for example, by the NARMS for their monitoring of retail meat, food animals and humans. However, enterococci are generally not considered important pathogens outside the hospitals and healthcare settings, due to which studies reporting enterococci and their AR from the environment are scarce. Studies on water sources are focused either on human-specific species, *E. faecalis* and *E. faecium*, on certain antimicrobial agents, such as vancomycin, or on polluted water environments such as hospital-impacted wastewater and agricultural runoff (Sadowy and Luczkiewicz 2014; Nishiyama *et al.* 2015; Young *et al* 2016). Prevalence and persistence of AR enterococci released into surface water are of particular interest not only because they can spread to different environments and increase the chance of exposure to these bacteria through water-related activities but also because they can transfer AR genes to other bacterial species of higher human health concern. Studies that address the specific origin of AR enterococci in aquatic environments, their survival mechanisms in such environments and the transfer of AR genes are needed in addition to identifying potential environmental reservoirs of AR enterococci.

Conclusion

The environment is one of the three pillars of the One Health but also the least studied sector among the three. This review discussed the prevalence and diversity of pathogenic and commensal bacteria, namely *Salmonella*, *E. coli* and *Enterococcus*, present in surface waters and provided a basic understanding of the occurrence and persistence of AR in these bacteria. The widespread distribution of pathogenic and AR bacteria in surface waters of both developing and developed countries demonstrated the importance of environmental waters as a reservoir for these bacteria. Since AR pathogens present an increasing public health challenge worldwide, much more attention needs to be given on persisting as well as emerging AR in the environmental water, which is essential for better understanding the AR in humans and animals and thus the overall trend in AR.

Acknowledgements

This work was supported by the US Department of Agriculture (6040-32000-009-00-D), and the Centers for Disease Control and Prevention (Broad Agency Announcement to address antibiotic resistance, Agricultural Research Service Sub-Project Number: 6040-32000-009-08-R).

Conflict of Interest

No conflict of interest declared.

References

Aarestrup, F.M. and Wegener, H.C. (1999) The effects of antibiotic usage in food animals on the development of antimicrobial resistance of importance for humans in *Campylobacter* and *Escherichia coli*. *Microbes Infect* **1**, 639–644.

Agga, G.E., Arthur, T.M., Durso, L.M., Harhay, D.M. and Schmidt, J.W. (2015) Antimicrobial-resistant bacterial populations and antimicrobial resistance genes obtained from environments impacted by livestock and municipal waste. *PLoS ONE* **10**, e0132586.

Ahammad, Z.S., Sreekrishnan, T.R., Hands, C.L., Knapp, C.W. and Graham, D.W. (2014) Increased waterborne blaNDM-1 resistance gene abundances associated with seasonal human pilgrimages to the upper ganges river. *Environ Sci Technol* **48**, 3014–3020.

Ailes, E., Budge, P., Shankar, M., Collier, S., Brinton, W., Cronquist, A., Chen, M., Thornton, A. *et al.* (2013) Economic and health impacts associated with a *Salmonella* Typhimurium drinking water outbreak-Alamosa, CO, 2008. *PLoS ONE* **8**, e57439.

Alanis, A.J. (2005) Resistance to antibiotics: are we in the post-antibiotic era? *Arch Med Res* **36**, 697–705.

Alipour, M., Hajiesmaili, R., Talebjannat, M. and Yahyapour, Y. (2014) Identification and antimicrobial resistance of *Enterococcus* spp. isolated from the river and coastal waters in northern Iran. *ScientificWorldJ* **2014**, 287458.

Aminov, R.I. (2010) A brief history of the antibiotic era: lessons learned and challenges for the future. *Front Microbiol* **1**, 134.

Arai, N., Sekizuka, T., Tamamura, Y., Tanaka, K., Barco, L., Izumiya, H., Kusumoto, M., Hinenoya, A. *et al.* (2018) Phylogenetic characterization of *Salmonella enterica* Serovar Typhimurium and its monophasic variant isolated from food animals in japan revealed replacement of major epidemic clones in the last 4 decades. *J Clin Microbiol* **56**.

Arias, C.A. and Murray, B.E. (2012) The rise of the *Enterococcus*: beyond vancomycin resistance. *Nat Rev Microbiol* **10**, 266–278.

Assawatheptawee, K., Tansawai, U., Kiddee, A., Thongngen, P., Punyadi, P., Romgaew, T., Kongthai, P., Sumpradit, T. *et al.* (2017) Occurrence of extended-spectrum and AmpC-Type beta-lactamase genes in *Escherichia coli* isolated from water environments in Northern Thailand. *Microbes Environ* **32**, 293–296.

Auld, H., MacIver, D. and Klaassen, J. (2004) Heavy rainfall and waterborne disease outbreaks: the Walkerton example. *J Toxicol Environ Health A* **67**, 1879–1887.

AVMA (2008) *One Health: A New Professional Imperative. One Health Initiative Task Force Final Report*. Schaumburg, IL: American Veterinary Medical Association.

Badgley, B.D., Nayak, B.S. and Harwood, V.J. (2010) The importance of sediment and submerged aquatic vegetation as potential habitats for persistent strains of enterococci in a subtropical watershed. *Water Res* **44**, 5857–5866.

Bager, F., Aarestrup, F.M., Madsen, M. and Wegener, H.C. (1999) Glycopeptide resistance in *Enterococcus faecium* from broilers and pigs following discontinued use of avoparcin. *Microb Drug Resist* **5**, 53–56.

Bager, F., Madsen, M., Christensen, J. and Aarestrup, F.M. (1997) Avoparcin used as a growth promoter is associated with the occurrence of vancomycin-resistant *Enterococcus faecium* on Danish poultry and pig farms. *Prev Vet Med* **31**, 95–112.

Bajaj, P., Singh, N.S., Kanaujia, P.K. and Virdi, J.S. (2015) Distribution and molecular characterization of genes encoding CTX-M and AmpC beta-lactamases in *Escherichia coli* isolated from an Indian urban aquatic environment. *Sci Total Environ* **505**, 350–356.

Bartholomew, M.L., Heffernan, R.T., Wright, J.G., Klos, R.F., Monson, T., Khan, S., Trees, E., Sabol, A. *et al.* (2014) Multistate outbreak of *Salmonella enterica* serotype enteritidis infection associated with pet guinea pigs. *Vector Borne Zoonotic Dis* **14**, 414–421.

Basler, C., Nguyen, T.A., Anderson, T.C., Hancock, T. and Behravesh, C.B. (2016) Outbreaks of human salmonella infections associated with live poultry, United States, 1990–2014. *Emerg Infect Dis* **22**, 1705–1711.

Beach, M. (2004) Outbreaks associated with recreational water use: what can we learn from reporting systems and outbreak investigations in the United States? *Epidemiology* **15**, S214.

Benedict, K.M., Reses, H., Vigar, M., Roth, D.M., Roberts, V.A., Mattioli, M., Cooley, L.A., Hilborn, E.D. *et al.* (2017) Surveillance for Waterborne disease outbreaks associated with drinking water — United States, 2013–2014. *MMWR Morb Mortal Wkly Rep* **66**, 1216–1221.

Bhan, M.K., Bahl, R. and Bhatnagar, S. (2005) Typhoid and paratyphoid fever. *The Lancet* **366**, 749–762.

Blaak, H., de Kruijf, P., Hamidjaja, R.A., van Hoek, A.H., de Roda Husman, A.M. and Schets, F.M. (2014) Prevalence and characteristics of ESBL-producing *E. coli* in Dutch recreational waters influenced by wastewater treatment plants. *Vet Microbiol* **171**, 448–459.

Blanch, A.R., Caplin, J.L., Iversen, A., Kühn, I., Manero, A., Taylor, H.D. and Vilanova, X. (2003) Comparison of enterococcal populations related to urban and hospital wastewater in various climatic and geographic European regions. *J Appl Microbiol* **94**, 994–1002.

Bosch, S., Tauxe, R.V. and Behravesh, C.B. (2016) Turtle-associated Salmonellosis, United States, 2006–2014. *Emerg Infect Dis* **22**, 1149–1155.

Brooks, J.T., Rowe, S.Y., Shillam, P., Heltzel, D.M., Hunter, S.B., Slutsker, L., Hoekstra, R.M. and Luby, S.P. (2001) *Salmonella* Typhimurium infections transmitted by chlorine-pretreated clover sprout seeds. *Am J Epidemiol* **154**, 1020–1028.

Byappanahalli, M., Fowler, M., Shively, D. and Whitman, R. (2003) Ubiquity and persistence of *Escherichia coli* in a Midwestern coastal stream. *Appl Environ Microbiol* **69**, 4549–4555.

Cabelli, V.J. (1983) *Health Effects Criteria for Marine Recreational Waters*. Research Triangle Park, NC: U.S.E.P. Agency.

Cabral, J.P. (2010) Water microbiology. Bacterial pathogens and water. *Int J Environ Res Public Health* **7**, 3657–3703.

Canton, R. and Coque, T.M. (2006) The CTX-M beta-lactamase pandemic. *Curr Opin Microbiol* **9**, 466–475.

Catalao Dionisio, L.P., Joao, M., Ferreiro, V.S., Fidalgo, M.L., García Rosado, M.E. and Borrego, J.J. (2000) Occurrence of *Salmonella* spp in estuarine and coastal waters of Portugal. *Antonie Van Leeuwenhoek* **78**, 99–106.

CDC (2002) Outbreak of multidrug-resistant Salmonella Newport – United States, January–April 2002. *MMWR Morb Mortal Wkly Rep* **51**, 545–548.

CDC (2013) Vital signs: carbapenem-resistant Enterobacteriaceae. *MMWR Morb Mortal Wkly Rep* **62**, 165–170.

CDC (2016) *Escherichia coli* (*E. coli*). Atlanta, GA: U.S. Department of Health and Human Services, CDC.

CDC (2017) *Foodborne Diseases Active Surveillance Network (FoodNet): FoodNet 2015 Surveillance Report (Final Data)*. Atlanta, GA: U.S. Department of Health and Human Services, CDC.

CDC (2018a) *National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS): Human Isolates Surveillance Report for 2015 (Final Report)*. Atlanta, GA: US Department of Health and Human Services, CDC.

CDC (2018b) *National Salmonella Surveillance Annual Report, 2016*. Atlanta, GA: US Department of Health and Human Services, CDC.

CDC (2019) *Antibiotic Resistance Threats in the United States, 2019*. Atlanta, GA: U.S. Department of Health and Human Services, CDC.

Charatan, F. (1999) New York outbreak of *E. coli* poisoning affects 1000 and kills two. *BMJ* **319**, 873–873. https://doi.org/10.1136/bmj.319.7214.873a.

Chatham-Stephens, K., Medalla, F., Hughes, M., Appiah, G.D., Aubert, R.D., Caidi, H., Angelo, K.M., Walker, A.T. *et al.* (2019) Emergence of extensively drug-resistant *Salmonella* Typhi infections among travelers to or from Pakistan - United States, 2016–2018. *MMWR Morb Mortal Wkly Rep* **68**, 11–13.

Chen, Z., Yu, D., He, S., Ye, H., Zhang, L., Wen, Y., Zhang, W., Shu, L. *et al.* (2017) Prevalence of antibiotic-resistant *Escherichia coli* in drinking water sources in Hangzhou City. *Front Microbiol* **8**, 1133.

Cho, S., Hiott, L.M., Barrett, J.B., McMillan, E.A., House, S.L., Humayoun, S.B., Adams, E.S., Jackson, C.R. *et al.* (2018) Prevalence and characterization of *Escherichia coli* isolated from the Upper Oconee Watershed in Northeast Georgia. *PLoS ONE* **13**, e0197005.

Cho, S., Nguyen, H.A.T., McDonald, J.M., Woodley, T.A., Hiott, L.M., Barrett, J.B., Jackson, C.R. and Frye, J.G. (2019a) Genetic characterization of antimicrobial resistant *Escherichia coli* isolated from a mixed-use watershed in Northeast Georgia. *Int J Environ Res Public Health* **16**, 3761.

Cho, S., Hiott, L.M., McDonald, J.M., Barrett, J.B., McMillan, E.A., House, S.L., Adams, E.S., Frye, J.G. *et al.* (2019b) Diversity and antimicrobial resistance of *Enterococcus* from the Upper Oconee Watershed, Georgia. *J Appl Microbiol* **128**, 1221–1233.

Cho, S., Gupta, S.K., McMillan, E.A., Sharma, P., Ramadan, H., Jové, T., Jackson, C.R. and Frye, J.G. (in press) Whole genome sequence analysis of multidrug resistant *E. coli* isolated from surface water in Northeast Georgia, USA, including a ST131 epidemic strain with a phage-like plasmid encoding a blaCTX-M-15 extended spectrum beta-lactamase gene. *Microb Drug Resist* https://doi.org/10.1089/mdr.2019.0306.

Choi, S.H., Lee, S.O., Kim, T.H., Chung, J.W., Choo, E.J., Kwak, Y.G., Kim, M.N., Kim, Y.S. *et al.* (2004) Clinical features and outcomes of bacteremia caused by *Enterococcus casseliflavus* and *Enterococcus gallinarum*: analysis of 56 cases. *Clin Infect Dis* **38**, 53–56.

Clark, N.C., Teixeira, L.M., Facklam, R.R. and Tenover, F.C. (1998) Detection and differentiation of vanC-1, vanC-2, and vanC-3 glycopeptide resistance genes in enterococci. *J Clin Microbiol* **36**, 2294–2297.

Clarkson, L.S., Tobin-D'Angelo, M., Shuler, C., Hanna, S., Benson, J. and Voetsch, A.C. (2010) Sporadic *Salmonella enterica* serotype Javiana infections in Georgia and Tennessee: a hypothesis-generating study. *Epidemiol Infect* **138**, 340–346.

Collins, M.D., Jones, D., Farrow, J.A.E., Kilpper-Balz, R. and Schleifer, K.H. (1984) *Enterococcus avium* nom. rev., comb. nov.; *E. casseliflavus* nom. rev., comb. nov.; *E. durans* nom. rev., comb. nov.; *E. gallinarum* comb. nov.; and *E. malodoratus* sp. nov. *Int J Syst Evol Bacteriol* **34**, 220–223.

Contreras, G.A., DiazGranados, C.A., Cortes, L., Reyes, J., Vanegas, S., Panesso, D., Rincon, S., Diaz, L. *et al.* (2008) Nosocomial outbreak of *Enteroccocus gallinarum*: untaming of rare species of enterococci. *J Hosp Infect* **70**, 346–352.

Cooley, M., Carychao, D., Crawford-Miksza, L., Jay, M.T., Myers, C., Rose, C., Keys, C., Farrar, J. *et al.* (2007) Incidence and tracking of *Escherichia coli* O157:H7 in a major produce production region in California. *PLoS ONE* **2**, e1159.

Cooley, M.B., Quinones, B., Oryang, D., Mandrell, R.E. and Gorski, L. (2014) Prevalence of shiga toxin producing *Escherichia coli*, *Salmonella enterica*, and *Listeria monocytogenes* at public access watershed sites in a California Central Coast agricultural region. *Front Cell Infect Microbiol* **4**, 30.

Cooper, M.P., Lessa, F., Brems, B., Shoulson, R., York, S., Peterson, A., Noble-Wang, J., Duffy, R. *et al.* (2008) Outbreak of *Enterococcus gallinarum* infections after total knee arthroplasty. *Infect Control Hosp Epidemiol* **29**, 361–363.

Coque, T.M., Novais, A., Carattoli, A., Poirel, L., Pitout, J., Peixe, L., Baquero, F., Cantón, R. *et al.* (2008) Dissemination of clonally related *Escherichia coli* strains expressing extended-spectrum beta-lactamase CTX-M-15. *Emerg Infect Dis* **14**, 195–200.

Corso, A., Faccone, D., Gagetti, P., Togneri, A., Lopardo, H., Melano, R., Rodriguez, V., Rodriguez, M. *et al.* (2005) First report of VanA *Enterococcus gallinarum* dissemination within an intensive care unit in Argentina. *Int J Antimicrob Agents* **25**, 51–56.

Craun, G.F., Brunkard, J.M., Yoder, J.S., Roberts, V.A., Carpenter, J., Wade, T., Calderon, R.L., Roberts, J.M. *et al.* (2010) Causes of outbreaks associated with drinking water in the United States from 1971 to 2006. *Clin Microbiol Rev* **23**, 507–528.

Craun, G.F., Calderon, R.L. and Craun, M.F. (2005) Outbreaks associated with recreational water in the United States. *Int J Environ Health Res* **15**, 243–262.

Craun, M.F., Craun, G.F., Calderon, R.L. and Beach, M.J. (2006) Waterborne outbreaks reported in the United States. *J Water Health* **4**, 19–30.

Croxen, M.A., Law, R.J., Scholz, R., Keeney, K.M., Wlodarska, M. and Finlay, B.B. (2013) Recent advances in understanding enteric pathogenic *Escherichia coli*. *Clin Microbiol Rev* **26**, 822–880.

Crump, J.A., Luby, S.P. and Mintz, E.D. (2004) The global burden of typhoid fever. *Bull World Health Organ* **82**, 346–353.

Crump, J.A., Sjolund-Karlsson, M., Gordon, M.A. and Parry, C.M. (2015) Epidemiology, clinical presentation, laboratory diagnosis, antimicrobial resistance, and antimicrobial management of invasive salmonella infections. *Clin Microbiol Rev* **28**, 901–937.

de Perio, M.A., Yarnold, P.R., Warren, J. and Noskin, G.A. (2006) Risk factors and outcomes associated with non-*Enterococcus faecalis*, non-*Enterococcus faecium* enterococcal bacteremia. *Infect Control Hosp Epidemiol* **27**, 28–33.

DeFlorio-Barker, S., Wing, C., Jones, R.M. and Dorevitch, S. (2018) Estimate of incidence and cost of recreational waterborne illness on United States surface waters. *Environ Health* **17**, 3.

Denno, D.M., Keene, W.E., Hutter, C.M., Koepsell, J.K., Patnode, M., Flodin-Hursh, D., Stewart, L.K., Duchin, J.S. *et al.* (2009) Tri-county comprehensive assessment of risk factors for sporadic reportable bacterial enteric infection in children. *J Infect Dis* **199**, 467–476.

Dewey-Mattia, D., Manikonda, K., Hall, A.J., Wise, M.E. and Crowe, S.J. (2018) Surveillance for foodborne disease outbreaks — United States, 2009–2015. *MMWR Surveill Summ* **67**, 1–11.

Diab, M., Hamze, M., Bonnet, R., Saras, E., Madec, J.Y. and Haenni, M. (2018) Extended-spectrum beta-lactamase (ESBL)- and carbapenemase-producing Enterobacteriaceae in water sources in Lebanon. *Vet Microbiol* **217**, 97–103.

Dolejska, M., Bierosova, B., Kohoutova, L., Literak, I. and Cizek, A. (2009) Antibiotic-resistant Salmonella and *Escherichia coli* isolates with integrons and extended-spectrum beta-lactamases in surface water and sympatric black-headed gulls. *J Appl Microbiol* **106**, 1941–1950.

Domig, K.J., Mayer, H.K. and Kneifel, W. (2003) Methods used for the isolation, enumeration, characterisation and identification of *Enterococcus* spp. *Int J Food Microbiol* **88**, 165–188.

Dufour, A.P. (1984) *Health Effects Criteria for Fresh Recreational*. Cincinnati, OH: U.S.E.P. Agency.

Dutka-Malen, S., Blaimont, B., Wauters, G. and Courvalin, P. (1994) Emergence of high-level resistance to glycopeptides in *Enterococcus gallinarum* and *Enterococcus casseliflavus*. *Antimicrob Agents Chemother* **38**, 1675–1677.

Fairbrother, J.M. and Nadeau, E. (2006) *Escherichia coli*: on-farm contamination of animals. *Rev Sci Tech* **25**, 555–569.

Fang, H., Ohlsson, A.K., Ullberg, M. and Ozenci, V. (2012) Evaluation of species-specific PCR, Bruker MS, VITEK MS and the VITEK 2 system for the identification of clinical Enterococcus isolates. *Eur J Clin Microbiol Infect Dis* **31**, 3073–3077.

FDA (2012) *The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals. Guidance for Industry #209*. Rockville, MD: FDA.

FDA (2013a) *National Antimicrobial Resistance Monitoring System- Enteric Bacteria (NARMS): 2011 Retail Meat Annual Report*. Rockville, MD: U.S. Department of Health and Humans Services, FDA.

FDA (2013b) *National Antimicrobial Resistance Monitoring System- Enteric Bacteria (NARMS): 2011 Executive Report*. Rockville, MD: U.S. Department of Health and Humans Services, FDA.

Ferguson, D.M., Griffith, J.F., McGee, C.D., Weisberg, S.B. and Hagedorn, C. (2013) Comparison of *Enterococcus* species diversity in marine water and wastewater using Enterolert and EPA Method 1600. *J Environ Public Health* **2013**, 848049.

Fisher, K. and Phillips, C. (2009) The ecology, epidemiology and virulence of Enterococcus. *Microbiology* **155**, 1749–1757.

Foley, S.L. and Lynne, A.M. (2008) Food animal-associated Salmonella challenges: pathogenicity and antimicrobial resistance. *J Anim Sci* **86**, E173–187.

Folster, J.P., Pecic, G., Bolcen, S., Theobald, L., Hise, K., Carattoli, A., Zhao, S., McDermott, P.F. *et al.* (2010) Characterization of extended-spectrum cephalosporin-resistant *Salmonella enterica* serovar Heidelberg isolated from humans in the United States. *Foodborne Pathog Dis* **7**, 181–187.

Frye, J.G. and Jackson, C.R. (2013) Genetic mechanisms of antimicrobial resistance identified in *Salmonella enterica*, *Escherichia coli*, and Enteroccocus spp. isolated from U.S. food animals. *Front Microbiol* **4**, 135.

Fujioka, R., Sian-Denton, C., Borja, M., Castro, J. and Morphew, K. (1999) Soil: the environmental source of *Escherichia coli* and enterococci in Guam's streams. *J Appl Microbiol* **85**, 83S–89S.

Gold, H.S. (2001) Vancomycin-resistant enterococci: mechanisms and clinical observations. *Clin Infect Dis* **33**, 210–219.

Gordon, D.M., Bauer, S. and Johnson, J.R. (2002) The genetic structure of *Escherichia coli* populations in primary and secondary habitats. *Microbiology* **148**, 1513–1522.

Graciaa, D.S., Cope, J.R., Roberts, V.A., Cikesh, B.L., Kahler, A.M., Vigar, M., Hilborn, E.D., Wade, T.J. *et al.* (2018) Outbreaks associated with untreated recreational water — United States, 2000–2014. *MMWR Morb Mortal Wkly Rep* **67**, 701–706.

Green, M., Barbadora, K. and Michaels, M. (1991) Recovery of vancomycin-resistant gram-positive cocci from pediatric liver transplant recipients. *J Clin Microbiol* **29**, 2503–2506.

Grimont, P.A.D. and Weill, F.X. (2007) *Antigenic Formulae of the Salmonella Serovars*, 9th ed. Paris: WHO Collaborating Centre for Reference and Research on Salmonella, Institut Pasteur.

Guo, X., van Iersel, M.W., Chen, J., Brackett, R.E. and Beuchat, L.R. (2002) Evidence of association of salmonellae with tomato plants grown hydroponically in inoculated nutrient solution. *Appl Environ Microbiol* **68**, 3639–3643.

Guzman Prieto, A.M., van Schaik, W., Rogers, M.R., Coque, T.M., Baquero, F., Corander, J. and Willems, R.J. (2016) Global emergence and dissemination of enterococci as nosocomial pathogens: attack of the clones? *Front Microbiol* **7**, 788.

Haley, B.J., Cole, D.J. and Lipp, E.K. (2009) Distribution, diversity, and seasonality of waterborne salmonellae in a rural watershed. *Appl Environ Microbiol* **75**, 1248–1255.

Hamelin, K., Bruant, G., El-Shaarawi, A., Hill, S., Edge, T.A., Bekal, S., Fairbrother, J.M., Harel, J. *et al.* (2006) A virulence and antimicrobial resistance DNA microarray detects a high frequency of virulence genes in *Escherichia coli* isolates from Great Lakes recreational waters. *Appl Environ Microbiol* **72**, 4200–4206.

Hamelin, K., Bruant, G., El-Shaarawi, A., Hill, S., Edge, T.A., Fairbrother, J., Harel, J., Maynard, C. *et al.* (2007) Occurrence of virulence and antimicrobial resistance genes in *Escherichia coli* isolates from different aquatic ecosystems within the St. Clair River and Detroit River areas. *Appl Environ Microbiol* **73**, 477–484.

Hanning, I.B., Nutt, J.D. and Ricke, S.C. (2009) Salmonellosis outbreaks in the United States due to fresh produce: sources and potential intervention measures. *Foodborne Pathog Dis* **6**, 635–648.

Harwood, V.J., Brownell, M., Perusek, W. and Whitlock, J.E. (2001) Vancomycin-resistant *Enterococcus* spp. isolated from wastewater and chicken feces in the United States. *Appl Environ Microbiol* **67**, 4930–4933.

Haymaker, J., Sharma, M., Parveen, S., Hashem, F., May, E.B., Handy, E.T., White, C., East, C. *et al.* (2019) Prevalence of Shiga-toxigenic and atypical enteropathogenic *Escherichia coli* in untreated surface water and reclaimed water in the Mid-Atlantic U.S. *Environ Res* **172**, 630–636.

Helms, M., Vastrup, P., Gerner-Smidt, P. and Molbak, K. (2002) Excess mortality associated with antimicrobial drug-resistant Salmonella Typhimurium. *Emerg Infect Dis* **8**, 490–495.

Herikstad, H., Motarjemi, Y. and Tauxe, R.V. (2002) Salmonella surveillance: a global survey of public health serotyping. *Epidemiol Infect* **129**, 1–8.

Herman, K.M., Hall, A.J. and Gould, L.H. (2015) Outbreaks attributed to fresh leafy vegetables, United States, 1973–2012. *Epidemiol Infect* **143**, 3011–3021.

Hlavsa, M.C., Cikesh, B.L., Roberts, V.A., Kahler, A.M., Vigar, M., Hilborn, E.D., Wade, T.J., Roellig, D.M. *et al.* (2018) Outbreaks associated with treated recreational water — United States, 2000–2014. *MMWR Morb Mortal Wkly Rep* **67**, 547–551.

Holmes, A.H., Moore, L.S.P., Sundsfjord, A., Steinbakk, M., Regmi, S., Karkey, A., Guerin, P.J. and Piddock, L.J.V. (2016) Understanding the mechanisms and drivers of antimicrobial resistance. *The Lancet* **387**, 176–187.

Holt, P.S., Geden, C.J., Moore, R.W. and Gast, R.K. (2007) Isolation of *Salmonella enterica* serovar Enteritidis from houseflies (*Musca domestica*) found in rooms containing Salmonella serovar Enteritidis-challenged hens. *Appl Environ Microbiol* **73**, 6030–6035.

Hrudey, S.E., Payment, P., Huck, P.M., Gillham, R.W. and Hrudey, E.J. (2003) A fatal waterborne disease epidemic in Walkerton, Ontario: comparison with other waterborne outbreaks in the developed world. *Water Sci Technol* **47**, 7–14.

Hu, Y.Y., Cai, J.C., Zhou, H.W., Chi, D., Zhang, X.F., Chen, W.L., Zhang, R. and Chen, G.X. (2013) Molecular typing of CTX-M-producing *Escherichia coli* isolates from environmental water, swine feces, specimens from healthy humans, and human patients. *Appl Environ Microbiol* **79**, 5988–5996.

Hussein, H.S. and Sakuma, T. (2005) Prevalence of shiga toxin-producing *Escherichia coli* in dairy cattle and their products. *J Dairy Sci* **88**, 450–465.

Ishii, S., Hansen, D.L., Hicks, R.E. and Sadowsky, M. (2007) Beach sand and sediments are temporal sinks and sources of *Escherichia coli* in Lake Superior. *Environ Sci Technol* **41**, 2203–2209.

Ishii, S., Ksoll, W.B., Hicks, R.E. and Sadowsky, M.J. (2006) Presence and growth of naturalized *Escherichia coli* in temperate soils from Lake Superior watersheds. *Appl Environ Microbiol* **72**, 612–621.

Issenhuth-Jeanjean, S., Roggentin, P., Mikoleit, M., Guibourdenche, M., de Pinna, E., Nair, S., Fields, P.I. and Weill, F.X. (2014) Supplement 2008–2010 (no. 48) to the White-Kauffmann-Le Minor scheme. *Res Microbiol* **165**, 526–530.

Iversen, A., Kuhn, I., Franklin, A. and Mollby, R. (2002) High prevalence of vancomycin-resistant enterococci in Swedish sewage. *Appl Environ Microbiol* **68**, 2838–2842.

Jackson, B.R., Griffin, P.M., Cole, D., Walsh, K.A. and Chai, S.J. (2013) Outbreak-associated *Salmonella enterica* serotypes and food Commodities, United States, 1998–2008. *Emerg Infect Dis* **19**, 1239–1244.

Jackson, C.R., Fedorka-Cray, P.J. and Barrett, J.B. (2004) Use of a genus- and species-specific multiplex PCR for identification of enterococci. *J Clin Microbiol* **42**, 3558–3565.

Jackson, C.R., Fedorka-Cray, P.J., Jackson-Hall, M.C. and Hiott, L.M. (2005) Effect of media, temperature and culture conditions on the species population and antibiotic resistance of enterococci from broiler chickens. *Lett Appl Microbiol* **41**, 262–268.

Jett, B.D., Huycke, M.M. and Gilmore, M.S. (1994) Virulence of enterococci. *Clin Microbiol Rev* **7**, 462–478.

Johnson, J.R., Johnston, B., Clabots, C., Kuskowski, M.A. and Castanheira, M. (2010) *Escherichia coli* sequence type ST131 as the major cause of serious multidrug-resistant *E. coli* infections in the United States. *Clin Infect Dis* **51**, 286–294.

Jokinen, C.C., Schreier, H., Mauro, W., Taboada, E., Isaac-Renton, J.L., Topp, E., Edge, T., Thomas, J.E. *et al.* (2010) The occurrence and sources of Campylobacter spp., *Salmonella enterica* and *Escherichia coli* O157:H7 in the Salmon River, British Columbia, Canada. *J Water Health* **8**, 374–386.

Jokinen, C.C., Koot, J., Cole, L., Desruisseau, A., Edge, T.A., Khan, I.U., Koning, W., Lapen, D.R. *et al.* (2015) The distribution of *Salmonella enterica* serovars and subtypes in surface water from five agricultural regions across Canada. *Water Res* **76**, 120–131.

Jorgensen, S.B., Soraas, A.V., Arnesen, L.S., Leegaard, T.M., Sundsfjord, A. and Jenum, P.A. (2017) A comparison of extended spectrum beta-lactamase producing *Escherichia coli* from clinical, recreational water and wastewater

samples associated in time and location. *PLoS ONE* **12**, e0186576.

Jyoti, A., Ram, S., Vajpayee, P., Singh, G., Dwivedi, P.D., Jain, S.K. and Shanker, R. (2010) Contamination of surface and potable water in South Asia by Salmonellae: culture-independent quantification with molecular beacon real-time PCR. *Sci Total Environ* **408**, 1256–1263.

Kaper, J.B., Nataro, J.P. and Mobley, H.L. (2004) Pathogenic *Escherichia coli*. *Nat Rev Microbiol* **2**, 123–140.

Karkman, A., Do, T.T., Walsh, F. and Virta, M.P.J. (2018) Antibiotic-resistance genes in waste water. *Trends Microbiol* **26**, 220–228.

Keene, W.E., McAnulty, J.M., Hoesly, F.C., Williams, L.P., Hedberg, K., Oxman, G.L., Barrett, T.J., Pfaller, M.A. *et al.* (1994) A swimming-associated outbreak of hemorrhagic colitis caused by *Escherichia coli* O157:H7 and *Shigella sonnei*. *N Engl J Med* **331**, 579–584.

Kenzaka, T., Tani, K. and Nasu, M. (2010) High-frequency phage-mediated gene transfer in freshwater environments determined at single-cell level. *ISME J* **4**, 648–659.

Kieffer, N., Poirel, L., Bessa, L.J., Barbosa-Vasconcelos, A.,da Costa, P.M. and Nordmann, P. (2016) VIM-1, VIM-34, and IMP-8 carbapenemase-producing *Escherichia coli* strains recovered from a Portuguese River. *Antimicrob Agents Chemother* **60**, 2585–2586.

Kittinger, C., Lipp, M., Folli, B., Kirschner, A., Baumert, R., Galler, H., Grisold, A.J., Luxner, J. *et al.* (2016) Enterobacteriaceae isolated from the River Danube: antibiotic resistances, with a focus on the presence of ESBL and carbapenemases. *PLoS ONE* **11**, e0165820.

Klare, I., Badstübner, D., Konstabel, C., Böhme, G., Claus, H. and Witte, W. (1999) Decreased incidence of vanA-type vancomycin-resistant Enterococci isolated from poultry meat and from fecal samples of humans in the community after discontinuation of avoparcin usage in animal husbandry. *Microb Drug Resist* **5**, 45–52.

Kohler, C.D. and Dobrindt, U. (2011) What defines extraintestinal pathogenic *Escherichia coli*? *Int J Med Microbiol* **301**, 642–647.

Kruse, H., Johansen, B.K., Rørvik, L.M. and Schaller, G. (1999) The use of avoparcin as a growth promoter and the occurrence of vancomycin-resistant *Enterococcus* species in Norwegian poultry and swine production. *Microb Drug Resist* **5**, 135–139.

Kühn, I. (2003) Comparison of enterococcal populations in animals, humans, and the environment - a European study. *Int J Food Microbiol* **88**, 133–145.

Lata, P., Ram, S., Agrawal, M. and Shanker, R. (2009) Enterococci in river Ganga surface waters: propensity of species distribution, dissemination of antimicrobial-resistance and virulence-markers among species along landscape. *BMC Microbiol* **9**, 140.

Lauber, C.L., Glatzer, L. and Sinsabaugh, R.L. (2003) Prevalence of pathogenic *Escherichia coli* in recreational waters. *J Great Lakes Res* **29**, 301–306.

Lavigne, J.P. and Blanc-Potard, A.B. (2008) Molecular evolution of *Salmonella enterica* serovar Typhimurium and pathogenic *Escherichia coli*: from pathogenesis to therapeutics. *Infect Genet Evol* **8**, 217–226.

Layton, B.A., Walters, S.P., Lam, L.H. and Boehm, A.B. (2010) *Enterococcus* species distribution among human and animal hosts using multiplex PCR. *J Appl Microbiol* **109**, 539–547.

Lebreton, F., Willems, R.J.L. and Gilmore, M.S. (2014) Enterococcus diversity, origins in nature, and gut colonization. In *Enterococci: From Commensals to Leading Causes of Drug Resistant Infection* ed. Gilmore, M.S., Clewell, D.B., Ike, Y. and Shankar, N. Boston: Massachusetts Eye and Ear Infirmary.

Lee, L.A., Puhr, N.D., Maloney, E.K., Bean, N.H. and Tauxe, R.V. (1994) Increase in antimicrobial-resistant Salmonella infections in the United States, 1989–1990. *J Infect Dis* **170**, 128–134.

Lemarchand, K. and Lebaron, P. (2003) Occurrence of *Salmonella* spp. and *Cryptosporidium* spp. in a French coastal watershed: relationship with faecal indicators. *FEMS Microbiol Lett* **218**, 203–209.

Levantesi, C., Bonadonna, L., Briancesco, R., Grohmann, E., Toze, S. and Tandoi, V. (2012) Salmonella in surface and drinking water: occurrence and water-mediated transmission. *Food Res Int* **45**, 587–602.

Levy, S.B. and Marshall, B. (2004) Antibacterial resistance worldwide: causes, challenges and responses. *Nat Med* **10**, S122–129.

Li, B., Vellidis, G., Liu, H., Jay-Russell, M., Zhao, S., Hu, Z., Wright, A. and Elkins, C.A. (2014) Diversity and antimicrobial resistance of *Salmonella enterica* isolates from surface water in Southeastern United States. *Appl Environ Microbiol* **80**, 6355–6365.

Liassine, N., Frei, R., Jan, I. and Auckenthaler, R. (1998) Characterization of glycopeptide-resistant enterococci from a Swiss hospital. *J Clin Microbiol* **36**, 1853–1858.

Lim, L.M., Ly, N., Anderson, D., Yang, J.C., Macander, L., Jarkowski, A. 3rd, Forrest, A., Bulitta, J.B. and *et al.* (2010) Resurgence of colistin: a review of resistance, toxicity, pharmacodynamics, and dosing. *Pharmacotherapy* **30**, 1279–1291.

Liu, Y.-Y., Wang, Y., Walsh, T.R., Yi, L.-X., Zhang, R., Spencer, J., Doi, Y., Tian, G. *et al.* (2016) Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. *Lancet Infect Dis* **16**, 161–168.

Luo, Z., Gu, G., Ginn, A., Giurcanu, M.C., Adams, P., Vellidis, G., van Bruggen, A.H., Danyluk, M.D. *et al.* (2015) Distribution and characterization of *Salmonella enterica* isolates from irrigation ponds in the Southeastern United States. *Appl Environ Microbiol* **81**, 4376–4387.

Lyimo, B., Buza, J., Subbiah, M., Smith, W. and Call, D.R. (2016) Comparison of antibiotic resistant *Escherichia coli*

obtained from drinking water sources in northern Tanzania: a cross-sectional study. *BMC Microbiol* **16**, 254.

Maal-Bared, R., Bartlett, K.H., Bowie, W.R. and Hall, E.R. (2013) Phenotypic antibiotic resistance of *Escherichia coli* and *E. coli* O157 isolated from water, sediment and biofilms in an agricultural watershed in British Columbia. *Sci Total Environ* **443**, 315–323.

Magill, S.S., O'Leary, E., Janelle, S.J., Thompson, D.L., Dumyati, G., Nadle, J., Wilson, L.E., Kainer, M.A. *et al.* (2018) Changes in prevalence of health care-associated infections in U.S. hospitals. *N Engl J Med* **379**, 1732–1744.

Maheux, A.F., Dion-Dupont, V., Bouchard, S., Bisson, M., Bergeron, M.G. and Rodriguez, M.J. (2015) Comparison of four β-glucuronidase and β-galactosidase-based commercial culture methods used to detect *Escherichia coli* and total coliforms in water. *J Water Health* **13**, 340–352.

Mahon, B.M., Brehony, C., McGrath, E., Killeen, J., Cormican, M., Hickey, P., Keane, S., Hanahoe, B. *et al.* (2017) Indistinguishable NDM-producing *Escherichia coli* isolated from recreational waters, sewage, and a clinical specimen in Ireland, 2016 to 2017. *Euro Surveill* **22**, pii: 30513.

Maron, D.F., Smith, T.J. and Nachman, K.E. (2013) Restrictions on antimicrobial use in food animal production: an international regulatory and economic survey. *Global Health* **9**, 1–11.

Martin, J.D. and Mundt, J.O. (1972) Enterococci in insects. *Appl Microbiol* **24**, 575–580.

Martinez, J.L. (2009) The role of natural environments in the evolution of resistance traits in pathogenic bacteria. *Proc Biol Sci* **276**, 2521–2530.

Marus, J.R., Magee, M.J., Manikonda, K. and Nichols, M.C. (2019) Outbreaks of *Salmonella enterica* infections linked to animal contact: demographic and outbreak characteristics and comparison to foodborne outbreaks-United States, 2009–2014. *Zoonoses Public Health* **66**, 370–376.

Mathys, D.A., Mollenkopf, D.F., Feicht, S.M., Adams, R.J., Albers, A.L., Stuever, D.M., Grooters, S.V., Ballash, G.A. *et al.* (2019) Carbapenemase-producing Enterobacteriaceae and *Aeromonas* spp. present in wastewater treatment plant effluent and nearby surface waters in the US. *PLoS ONE* **14**, e0218650.

Maurer, J.J., Martin, G., Hernandez, S., Cheng, Y., Gerner-Smidt, P., Hise, K.B., Tobin D'Angelo, M., Cole, D. *et al.* (2015) Diversity and persistence of *Salmonella enterica* strains in rural landscapes in the Southeastern United States. *PLoS ONE* **10**, e0128937.

McArthur, J.V., Fletcher, D.E., Tuckfield, R.C. and Baker-Austin, C. (2016) Patterns of multi-antibiotic-resistant *Escherichia coli* from streams with no history of antimicrobial inputs. *Microb Ecol* **72**, 840–850.

McCarthy, T.A., Barrett, N.L., Hadler, J.L., Salsbury, B., Howard, R.T., Dingman, D.W., Brinkman, C.D., Bibb, W.F. *et al.* (2001) Hemolytic-uremic syndrome and *Escherichia coli* O121 at a Lake in Connecticut, 1999. *Pediatrics* **108**, E59.

McDonald, L.C., Kuehnert, M.J., Tenover, F.C. and Jarvis, W.R. (1997) Vancomycin-resistant enterococci outside the health-care setting: prevalence, sources, and public health implications. *Emerg Infect Dis* **3**, 311–317.

McEgan, R., Chandler, J.C., Goodridge, L.D. and Danyluk, M.D. (2014) Diversity of Salmonella isolates from central Florida surface waters. *Appl Environ Microbiol* **80**, 6819–6827.

Meinersmann, R.J., Berrang, M.E., Jackson, C.R., Fedorka-Cray, P., Ladely, S., Little, E., Frye, J.G. and Mattsson, B. (2008) *Salmonella*, *Campylobacter* and *Enterococcus* spp.: their antimicrobial resistance profiles and their spatial relationships in a synoptic study of the Upper Oconee River basin. *Microb Ecol* **55**, 444–452.

Meric, G., Kemsley, E.K., Falush, D., Saggers, E.J. and Lucchini, S. (2013) Phylogenetic distribution of traits associated with plant colonization in *Escherichia coli*. *Environ Microbiol* **15**, 487–501.

Merquior, V.L., Goncalves Neves, F.P., Ribeiro, R.L., Duarte, R.S., de Andrade Marques, E. and Teixeira, L.M. (2008) Bacteraemia associated with a vancomycin-resistant *Enterococcus gallinarum* strain harbouring both the vanA and vanC1 genes. *J Med Microbiol* **57**, 244–245.

Mettee Zarecki, S.L., Bennett, S.D., Hall, J., Yaeger, J., Lujan, K., Adams-Cameron, M., Winpisinger Quinn, K., Brenden, R. *et al.* (2013) US outbreak of human Salmonella infections associated with aquatic frogs, 2008–2011. *Pediatrics* **131**, 724–731.

Molale, L.G. and Bezuidenhout, C.C. (2016) Antibiotic resistance, efflux pump genes and virulence determinants in *Enterococcus* spp. from surface water systems. *Environ Sci Pollut Res Int* **23**, 21501–21510.

Montezzi, L.F., Campana, E.H., Correa, L.L., Justo, L.H., Paschoal, R.P., da Silva, I.L., Souza Mdo, C., Drolshagen, M. *et al.* (2015) Occurrence of carbapenemase-producing bacteria in coastal recreational waters. *Int J Antimicrob Agents* **45**, 174–177.

Moore, D.F., Guzman, J.A. and McGee, C. (2008) Species distribution and antimicrobial resistance of enterococci isolated from surface and ocean water. *J Appl Microbiol* **105**, 1017–1025.

Mundt, J. (1963a) Occurrence of enterococci on plants in a wild environment. *J Appl Microbiol* **11**, 141–144.

Mundt, J.O. (1963b) Occurrence of enterococci in animals in a wild environment. *Appl Microbiol* **11**, 136–140.

Mundt, J.O. and Graham, W.F. (1968) *Streptococcus faecium* var. casselifavus, nov. var. *J Bacteriol* **95**, 2005–2009.

Nam, S., Kim, M.J., Park, C., Park, J.G., Maeng, P.J. and Lee, G.C. (2013) Detection and genotyping of vancomycin-resistant *Enterococcus* spp. by multiplex polymerase chain reaction in Korean aquatic environmental samples. *Int J Hyg Environ Health* **216**, 421–427.

Nataro, J.P. and Kaper, J.B. (1998) Diarrheagenic *Escherichia coli*. *Clin Microbiol Rev* **11**, 142–201.

Nation, R.L. and Li, J. (2009) Colistin in the 21st century. *Curr Opin Infect Dis* **22**, 535–543.

Natvig, E.E., Ingham, S.C., Ingham, B.H., Cooperband, L.R. and Roper, T.R. (2002) *Salmonella enterica* serovar Typhimurium and *Escherichia coli* contamination of root and leaf vegetables grown in soils with incorporated bovine manure. *Appl Environ Microbiol* **68**, 2737–2744.

Nicolas-Chanoine, M.H., Bertrand, X. and Madec, J.Y. (2014) *Escherichia coli* ST131, an intriguing clonal group. *Clin Microbiol Rev* **27**, 543–574.

Nicolas-Chanoine, M.H., Blanco, J., Leflon-Guibout, V., Demarty, R., Alonso, M.P., Canica, M.M., Park, Y.J., Lavigne, J.P. *et al*. (2008) Intercontinental emergence of *Escherichia coli* clone O25:H4-ST131 producing CTX-M-15. *J Antimicrob Chemother* **61**, 273–281.

Niemi, R.M., Ollinkangas, T., Paulin, L., Svec, P., Vandamme, P., Karkman, A., Kosina, M. and Lindstrom, K. (2012) *Enterococcus rivorum* sp. nov., from water of pristine brooks. *Int J Syst Evol Microbiol* **62**, 2169–2173.

Nishiyama, M., Iguchi, A. and Suzuki, Y. (2015) Identification of *Enterococcus faecium* and *Enterococcus faecalis* as vanC-type Vancomycin-Resistant Enterococci (VRE) from sewage and river water in the provincial city of Miyazaki, Japan. *J Environ Sci Health A Tox Hazard Subst Environ Eng* **50**, 16–25.

Novais, C., Coque, T.M., Ferreira, H., Sousa, J.C. and Peixe, L. (2005) Environmental contamination with vancomycin-resistant enterococci from hospital sewage in Portugal. *Appl Environ Microbiol* **71**, 3364–3368.

Olsen, S.J., Miller, G., Breuer, T., Kennedy, M., Higgins, C., Walford, J., McKee, G., Fox, K. *et al*. (2002) A waterborne outbreak of *Escherichia coli* O157:H7 infections and hemolytic uremic syndrome: implications for rural water systems. *Emerg Infect Dis* **8**, 370–375.

Padiglione, A.A., Grabsch, E.A., Olden, D., Hellard, M., Sinclair, M.I., Fairley, C.K. and Grayson, M.L. (2000) Fecal colonization with vancomycin-resistant enterococci in Australia. *Emerg Infect Dis* **6**, 534–536.

Parry, C.M. and Threlfall, E.J. (2008) Antimicrobial resistance in typhoidal and nontyphoidal salmonellae. *Curr Opin Infect Dis* **21**, 531–538.

Parte, A.C. (2018) LPSN - list of prokaryotic names with standing in nomenclature (bacterio.net), 20 years on. *Int J Syst Evol Microbiol* **68**, 1825–1829.

Patchanee, P., Molla, B., White, N., Line, D.E. and Gebreyes, W.A. (2010) Tracking salmonella contamination in various watersheds and phenotypic and genotypic diversity. *Foodborne Pathog Dis* **7**, 1113–1120.

Patel, R., Piper, K.E., Rouse, M.S., Steckelberg, J.M., Uhl, J.R., Kohner, P., Hopkins, M.K., Cockerill, F.R. III *et al*. (1998) Determination of 16S rRNA sequences of enterococci and application to species identification of nonmotile *Enterococcus gallinarum* isolates. *J Clin Microbiol* **36**, 3399–3407.

Paton, A.W. and Paton, J.C. (1998) Detection and characterization of Shiga toxigenic *Escherichia coli* by using multiplex PCR assays for stx1, stx2, eaeA, enterohemorrhagic *E. coli* hlyA, rfbO111, and rfbO157. *J Clin Microbiol* **36**, 598–602.

Petty, N.K., Ben Zakour, N.L., Stanton-Cook, M., Skippington, E., Totsika, M., Forde, B.M., Phan, M.D., Gomes Moriel, D. *et al*. (2014) Global dissemination of a multidrug resistant *Escherichia coli* clone. *Proc Natl Acad Sci USA* **111**, 5694–5699.

Philippon, A., Arlet, G. and Jacoby, G.A. (2002) Plasmid-determined AmpC-type beta-lactamases. *Antimicrob Agents Chemother* **46**, 1–11.

Picard, B., Garcia, J.S., Gouriou, S., Duriez, P., Brahimi, N., Bingen, E., Elion, J. and Denamur, E. (1999) The link between phylogeny and virulence in *Escherichia coli* extraintestinal infection. *Infect Immun* **67**, 546–553.

Pitout, J.D. (2012) Extraintestinal pathogenic *Escherichia coli*: A combination of virulence with antibiotic resistance. *Front Microbiol* **3**, 9.

Poirel, L., Barbosa-Vasconcelos, A., Simoes, R.R., Da Costa, P.M., Liu, W. and Nordmann, P. (2012) Environmental KPC-producing *Escherichia coli* isolates in Portugal. *Antimicrob Agents Chemother* **56**, 1662–1663.

Poole, K. (2004) Resistance to beta-lactam antibiotics. *Cell Mol Life Sci* **61**, 2200–2223.

Power, M.L., Littlefield-Wyer, J., Gordon, D.M., Veal, D.A. and Slade, M.B. (2005) Phenotypic and genotypic characterization of encapsulated *Escherichia coli* isolated from blooms in two Australian lakes. *Environ Microbiol* **7**, 631–640.

Probert, W.S., Miller, G.M. and Ledin, K.E. (2017) Contaminated stream water as source for *Escherichia coli* O157 illness in children. *Emerg Infect Dis* **23**, 1216–1218.

Proia, L., Anzil, A., Borrego, C., Farre, M., Llorca, M., Sanchis, J., Bogaerts, P., Balcazar, J.L. *et al*. (2018) Occurrence and persistence of carbapenemases genes in hospital and wastewater treatment plants and propagation in the receiving river. *J Hazard Mater* **358**, 33–43.

Ram, S., Vajpayee, P., Tripathi, U., Singh, R.L., Seth, P.K. and Shanker, R. (2008) Determination of antimicrobial resistance and virulence gene signatures in surface water isolates of *Escherichia coli*. *J Appl Microbiol* **105**, 1899–1908.

Ran, Q., Badgley, B.D., Dillon, N., Dunny, G.M. and Sadowsky, M.J. (2013) Occurrence, genetic diversity, and persistence of enterococci in a Lake Superior watershed. *Appl Environ Microbiol* **79**, 3067–3075.

Ratnam, S., March, S.B., Ahmed, R., Bezanson, G.S. and Kasatiya, S. (1988) Characterization of *Escherichia coli* serotype O157:H7. *J Clin Microbiol* **26**, 2006–2012.

Reid, K.C., Cockerill, F.R. III and Patel, R. (2001) Clinical and epidemiological features of *Enterococcus casseliflavus/flavescens* and *Enterococcus gallinarum* bacteremia: a report of 20 cases. *Clin Infect Dis* **32**, 1540–1546.

Resistance, R.o.A. (2014) *Antimicrobial Resistance: Tackling a Crisis for the Future Health and Wealth of Nations*.

Rice, E.W., Messer, J.W., Johnson, C.H. and Reasoner, D.J. (1995) Occurrence of high-level aminoglycoside resistance in environmental isolates of enterococci. *Appl Environ Microbiol* **61**, 374–376.

Rivera, S.C., Hazen, T.C. and Toranzos, G.A. (1988) Isolation of fecal coliforms from pristine sites in a tropical rain forest. *Appl Environ Microbiol* **54**, 513–517.

Robinson, T.P., Bu, D.P., Carrique-Mas, J., Fevre, E.M., Gilbert, M., Grace, D., Hay, S.I., Jiwakanon, J. *et al.* (2016) Antibiotic resistance is the quintessential One Health issue. *Trans R Soc Trop Med Hyg* **110**, 377–380.

Rosenberg Goldstein, R.E., Micallef, S.A., Gibbs, S.G., George, A., Claye, E., Sapkota, A., Joseph, S.W. and Sapkota, A.R. (2014) Detection of vancomycin-resistant enterococci (VRE) at four U.S. wastewater treatment plants that provide effluent for reuse. *Sci Total Environ* **466–467**, 404–411.

Rosenberg, M.L., Koplan, J.P., Wachsmuth, I.K., Wells, J.G., Gangarosa, E.J., Guerrant, R.L. and Sack, D.A. (1977) Epidemic diarrhea at Crater Lake from enterotoxigenic *Escherichia coli*. A large waterborne outbreak. *Ann Intern Med* **86**, 714–718.

Rossolini, G.M., Arena, F., Pecile, P. and Pollini, S. (2014) Update on the antibiotic resistance crisis. *Curr Opin Pharmacol* **18**, 56–60.

Runcharoen, C., Raven, K.E., Reuter, S., Kallonen, T., Paksanont, S., Thammachote, J., Anun, S., Blane, B. *et al.* (2017) Whole genome sequencing of ESBL-producing *Escherichia coli* isolated from patients, farm waste and canals in Thailand. *Genome Med* **9**, 81.

Sadowy, E. and Luczkiewicz, A. (2014) Drug-resistant and hospital-associated *Enterococcus faecium* from wastewater, riverine estuary and anthropogenically impacted marine catchment basin. *BMC Microbiol* **14**, 66.

Savageau, M.A. (1983) *Escherichia coli* habitats, cell types, and molecular mechanisms of gene control. *Am Nat* **122**, 732–744.

Schriewer, A., Miller, W.A., Byrne, B.A., Miller, M.A., Oates, S., Conrad, P.A., Hardin, D., Yang, H.H. *et al.* (2010) Presence of Bacteroidales as a predictor of pathogens in surface waters of the central California coast. *Appl Environ Microbiol* **76**, 5802–5814.

Schuster, C.J., Ellis, A.G., Robertson, W.J., Charron, D.F., Aramini, J.J., Marshall, B.J. and Medeiros, D.T. (2005) Infectious disease outbreaks related to drinking water in Canada, 1974–2001. *Can J Public Health* **96**, 254–258.

Schwarz, S. and Johnson, A.P. (2016) Transferable resistance to colistin: a new but old threat. *J Antimicrob Chemother* **71**, 2066–2070.

Sedlacek, I., Holochova, P., Maslanova, I., Kosina, M., Sproer, C., Bryndova, H., Vandamme, P., Rudolf, I. *et al.* (2013) *Enterococcus ureilyticus* sp. nov. and *Enterococcus rotai* sp. nov., two urease-producing enterococci from the environment. *Int J Syst Evol Microbiol* **63**, 502–510.

Servais, P. and Passerat, J. (2009) Antimicrobial resistance of fecal bacteria in waters of the Seine river watershed (France). *Sci Total Environ* **408**, 365–372.

Shen, Z., Wang, Y., Shen, Y., Shen, J. and Wu, C. (2016) Early emergence of mcr-1 in *Escherichia coli* from food-producing animals. *Lancet Infect Dis* **16**, 293.

Sidhu, J.P., Ahmed, W., Hodgers, L. and Toze, S. (2013) Occurrence of virulence genes associated with Diarrheagenic pathotypes in *Escherichia coli* isolates from surface water. *Appl Environ Microbiol* **79**, 328–335.

Sidhu, J.P., Hodgers, L., Ahmed, W., Chong, M.N. and Toze, S. (2012) Prevalence of human pathogens and indicators in stormwater runoff in Brisbane, Australia. *Water Res* **46**, 6652–6660.

Sidhu, J.P., Skelly, E., Hodgers, L., Ahmed, W., Li, Y. and Toze, S. (2014) Prevalence of enterococcus species and their virulence genes in fresh water prior to and after storm events. *Environ Sci Technol* **48**, 2979–2988.

Simental, L. and Martinez-Urtaza, J. (2008) Climate patterns governing the presence and permanence of salmonellae in coastal areas of Bahia de Todos Santos, Mexico. *Appl Environ Microbiol* **74**, 5918–5924.

Sistek, V., Maheux, A.F., Boissinot, M., Bernard, K.A., Cantin, P., Cleenwerck, I., De Vos, P. and Bergeron, M.G. (2012) *Enterococcus ureasiticus* sp. nov. and *Enterococcus quebecensis* sp. nov., isolated from water. *Int J Syst Evol Microbiol* **62**, 1314–1320.

Sjölund-Karlsson, M., Rickert, R., Matar, C., Pecic, G., Howie, R.L., Joyce, K., Medalla, F., Barzilay, E.J. *et al.* (2010) Salmonella isolates with decreased susceptibility to extended-spectrum cephalosporins in the United States. *Foodborne Pathog Dis* **7**, 1503–1509.

Somarelli, J.A., Makarewicz, J.C., Sia, R. and Simon, R. (2007) Wildlife identified as major source of *Escherichia coli* in agriculturally dominated watersheds by BOX A1R-derived genetic fingerprints. *J Environ Manage* **82**, 60–65.

Svec, P., Devriese, L.A., Sedlácek, I., Baele, M., Vancanneyt, M., Haesebrouck, F., Swings, J. and Doskar, J. (2001) *Enterococcus haemoperoxidus* sp. nov. and *Enterococcus moraviensis* sp. nov., isolated from water. *Int J Syst Evol Microbiol* **51**, 1567–1574.

Svec, P. and Sedlácek, I. (1999) occurrence of *Enterococcus* spp in waters. *Folia Microbiol (Praha)* **44**, 3–10.

Svec, P., Vancanneyt, M., Devriese, L.A., Naser, S.M., Snauwaert, C., Lefebvre, K., Hoste, B. and Swings, J. (2005) *Enterococcus aquimarinus* sp. nov., isolated from sea water. *Int J Syst Evol Microbiol* **55**, 2183–2187.

Svec, P., Vancanneyt, M., Sedlacek, I., Naser, S.M., Snauwaert, C., Lefebvre, K., Hoste, B. and Swings, J. (2006) *Enterococcus silesiacus* sp. nov. and *Enterococcus termitis* sp. nov. *Int J Syst Evol Microbiol* **56**, 577–581.

Tannock, G.W. and Cook, G. (2002) *The Enterococci: Pathogenesis, Molecular Biology, and Antibiotic Resistance*. Washington, DC: ASM Press.

Thaden, J.T., Lewis, S.S., Hazen, K.C., Huslage, K., Fowler, V.G. Jr, Moehring, R.W., Chen, L.F., Jones, C.D. *et al.* (2014) Rising rates of carbapenem-resistant enterobacteriaceae in community hospitals: a mixed-methods review of epidemiology and microbiology practices in a network of community hospitals in the southeastern United States. *Infect Control Hosp Epidemiol* **35**, 978–983.

Thomas, J.L., Slawson, R.M. and Taylor, W.D. (2013) Salmonella serotype diversity and seasonality in urban and rural streams. *J Appl Microbiol* **114**, 907–922.

Till, D., McBride, G., Ball, A., Taylor, K. and Pyle, E. (2008) Large-scale freshwater microbiological study: rationale, results and risks. *J Water Health* **6**, 443–460.

Titilawo, Y., Obi, L. and Okoh, A. (2015a) Antimicrobial resistance determinants of *Escherichia coli* isolates recovered from some rivers in Osun State, South-Western Nigeria: Implications for public health. *Sci Total Environ* **523**, 82–94.

Titilawo, Y., Obi, L. and Okoh, A. (2015b) Occurrence of virulence gene signatures associated with diarrhoeagenic and non-diarrhoeagenic pathovars of *Escherichia coli* isolates from some selected rivers in South-Western Nigeria. *BMC Microbiol* **15**, 204.

Toye, B., Shymanski, J., Bobrowska, M., Woods, W. and Ramotar, K. (1997) Clinical and epidemiological significance of enterococci intrinsically resistant to vancomycin (possessing the vanC genotype). *J Clin Microbiol* **35**, 3166–3170.

Travers, K. and Barza, M. (2002) Morbidity of infections caused by antimicrobial-resistant bacteria. *Clin Infect Dis* **34**, S131–S134.

U.S.EPA (1986) *Ambient Water Quality Criteria for Bacteria –* 1986th ed. Washington, DC: Office of Water, U.S.EPA.

U.S.EPA (2012) *Recreational Water Quality Criteria*. Washington, DC: Office of Water, U.S.EPA.

Varma, J.K., Molbak, K., Barrett, T.J., Beebe, J.L., Jones, T.F., Rabatsky-Ehr, T., Smith, K.E., Vugia, D.J. *et al.* (2005) Antimicrobial resistant nontyphoidal Salmonella is associated with excess bloodstream infections and hospitalizations. *J Infect Dis* **191**, 554–561.

Vereen, E. Jr, Lowrance, R.R., Jenkins, M.B., Adams, P., Rajeev, S. and Lipp, E.K. (2013) Landscape and seasonal factors influence Salmonella and Campylobacter prevalence in a rural mixed use watershed. *Water Res* **47**, 6075–6085.

Verma, A., Bolton, F.J., Fiefield, D., Lamb, P., Woloschin, E., Smith, N. and McCann, R. (2007) An outbreak of *E. coli* O157 associated with a swimming pool: an unusual vehicle of transmission. *Epidemiol Infect* **135**, 989–992.

Vila, J., Saez-Lopez, E., Johnson, J.R., Romling, U., Dobrindt, U., Canton, R., Giske, C.G., Naas, T. *et al.* (2016) *Escherichia coli*: an old friend with new tidings. *FEMS Microbiol Rev* **40**, 437–463.

Wade, T.J., Pai, N., Eisenberg, J.N.S. and Colford, J.M. (2003) Do US Environmental Protection Agency water quality guidelines for recreational waters prevent gastrointestinal illness? A systematic review and meta-analysis. *Environ Health Perspect* **111**, 1102–1109.

Walk, S.T., Alm, E.W., Calhoun, L.M., Mladonicky, J.M. and Whittam, T.S. (2007) Genetic diversity and population structure of *Escherichia coli* isolated from freshwater beaches. *Environ Microbiol* **9**, 2274–2288.

Walk, S.T., Alm, E.W., Gordon, D.M., Ram, J.L., Toranzos, G.A., Tiedje, J.M. and Whittam, T.S. (2009) Cryptic lineages of the genus *Escherichia*. *Appl Environ Microbiol* **75**, 6534–6544.

Walsh, T.R., Weeks, J., Livermore, D.M. and Toleman, M.A. (2011) Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study. *Lancet Infect Dis* **11**, 355–362.

Wei, Z., Xu, X., Yan, M., Chang, H., Li, Y., Kan, B. and Zeng, M. (2019) *Salmonella* Typhimurium and *Salmonella Enteritidis* infections in sporadic diarrhea in children: source tracing and resistance to third-generation cephalosporins and ciprofloxacin. *Foodborne Pathog Dis* **16**, 244–255.

Wendt, C., Krause, C., Xander, L.U., Löffler, D. and Floss, H. (1999) Prevalence of colonization with vancomycin-resistant enterococci in various population groups in Berlin, Germany. *J Hosp Infect* **42**, 193–200.

White, A.P., Sibley, K.A., Sibley, C.D., Wasmuth, J.D., Schaefer, R., Surette, M.G., Edge, T.A. and Neumann, N.F. (2011) Intergenic sequence comparison of *Escherichia coli* isolates reveals lifestyle adaptations but not host specificity. *Appl Environ Microbiol* **77**, 7620–7632.

WHO (2000) *WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food*. Geneva, Switzerland: WHO.

WHO (2013) *Integrated Surveillance of Antimicrobial Resistance: Guidance from a WHO Advisory Group*. Geneva, Switzerland: WHO.

WHO (2014) *Antimicrobial Resistance Global Report on Surveillance*. Geneva, Switzerland: WHO.

WHO (2019) *Critically Important Antimicrobials for Human Medicine*, 6th revision. Geneva, Switzerland: WHO.

WHO and UNICEF (2000) *Global Water Supply and Sanitation Assessment 2000 Report*. Geneva, Switzerland; New York, USA: World Health Organization (WHO); United Nations Children's Fund (UNICEF).

Winokur, P.L., Brueggemann, A., DeSalvo, D.L., Hoffmann, L., Apley, M.D., Uhlenhopp, E.K., Pfaller, M.A. and Doern, G.V. (2000) Animal and human multidrug-resistant, cephalosporin-resistant salmonella isolates expressing a plasmid-mediated CMY-2 AmpC beta-lactamase. *Antimicrob Agents Chemother* **44**, 2777–2783.

Xu, G., Jiang, Y., An, W., Wang, H. and Zhang, X. (2015) Emergence of KPC-2-producing *Escherichia coli* isolates in an urban river in Harbin, China. *World J Microbiol Biotechnol* **31**, 1443–1450.

Yang, F., Huang, L., Li, L., Yang, Y., Mao, D. and Luo, Y. (2017) Discharge of KPC-2 genes from the WWTPs contributed to their enriched abundance in the receiving river. *Sci Total Environ* **581–582**, 136–143.

Young, S., Nayak, B., Sun, S., Badgley, B.D., Rohr, J.R. and Harwood, V.J. (2016) Vancomycin-resistant enterococci and bacterial community structure following a sewage spill into an aquatic environment. *Appl Environ Microbiol* **82**, 5653–5660.

Yu, C.Y., Ang, G.Y., Chin, P.S., Ngeow, Y.F., Yin, W.F. and Chan, K.G. (2016) Emergence of mcr-1-mediated colistin resistance in *Escherichia coli* in Malaysia. *Int J Antimicrob Agents* **47**, 504–505.

Zhao, S., Qaiyumi, S., Friedman, S., Singh, R., Foley, S.L., White, D.G., McDermott, P.F., Donkar, T. *et al.* (2003) Characterization of *Salmonella enterica* Serotype Newport Isolated from Humans and Food Animals. *J Clin Microbiol* **41**, 5366–5371.

Zheng, J., Luo, Y., Reed, E., Bell, R., Brown, E.W. and Hoffmann, M. (2017) Whole-genome comparative analysis of *Salmonella enterica* serovar Newport strains reveals lineage-specific divergence. *Genome Biol Evol* **6**, 1047–1050.

Zurfuh, K., Poirel, L., Nordmann, P., Nuesch-Inderbinen, M., Hachler, H. and Stephan, R. (2016) Occurrence of the plasmid-borne mcr-1 colistin resistance gene in extended-spectrum-beta-lactamase-producing enterobacteriaceae in river water and imported vegetable samples in Switzerland. *Antimicrob Agents Chemother* **60**, 2594–2595.