



Climate Change: Any Dangers from Antimicrobial Resistant Bacteria?

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Abstract

Antimicrobial resistance represents a threat whereby micro-organisms (particularly bacteria) become resistant to antibiotics and disinfectants, thus complicating our ability to treat and prevent infections. This is often developed by sub-inhibitory exposures to such drugs and/or disinfectants, but it can be caused by (often negative) changes in the environment as a stress–response mechanism to environmental conditions, such as temperature, salinity, metals (potentially toxic elements), and organic pollutants.

Here, we explored possible mechanisms by which climate change could either directly (by changes in temperature and/or precipitation) or indirectly—such as shifts in human populations, disease vectors, agriculture, water availability, glaciation, and hydrology— affect the development or transfer of antimicrobial resistance in bacteria.

Keywords

Antibiotic resistance · Pollution · Pathogens · Agriculture · Water

Climate change is altering the earth’s atmosphere in several ways, being expected to generate altered air temperatures and lead to more extreme changes in precipitation across the globe. The worldwide average surface temperature has increased 0.74 °C over the last century (Rosenzweig et al. 2007). These effects are not anticipated to be

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geographically uniform, and have generated multiple changes, including altered frequencies of extreme weather conditions in different parts of the world. The most significant differences in air temperature and climate classification are predicted to occur at more northern latitudes. In comparison, precipitation increases are present at both extreme northern latitudes and also sporadically across regions of the equator, including parts of India, Saudi Arabia, and East Africa (Beck et al. 2018). These changes in climate will translate to altered conditions relevant to microbial growth, at the scale of both individual microorganisms and at the community level. These changes will be relevant to all forms of microbial life, including bacteria, fungi, and viruses.

Climate change will also impact human health, increasing the prevalence of heat related diseases and leading to altered migration patterns. There is limited discussion in the literature regarding the mechanisms through which climate change will alter the development or dissemination of antimicrobial resistance (AMR) in the environment. However, it has been mentioned that global warming contributes to antibiotic resistance (AR) in the environment (e.g., MacFadden et al. 2018). Rather than attempt to list all previous articles that have been published on the subject, we will instead discuss current issues involving AMR and how they may be impacted by climate change.

Both climate change and antimicrobial resistance have been recognised as interdisciplinary problems related to the “tragedy of the commons” (Singer et al. 2016)—in which individuals behave according to one’s self interests, but contrary to the common good of others. A major misconception exists that the development of AMR stems from bacterial exposure to antibiotics or synthetic antibacterial compounds; the extent of this can be argued. It has, however, become more evident that anthropogenic pressures accelerate the presence of AMR (Forsberg et al. 2014), but it can also be presumed that inherent changes in natural landscapes could contribute as well—although these changes may occur at a slower pace and their contribution may be more difficult to elucidate.

There is strong evidence demonstrating that pollution, even at relatively low concentrations, can produce shifts in bacterial communities (the “microbiome”). Resistance traits within a microbial community (i.e., the “resistome”) propagate in the presence of a natural selection factor, which ultimately creates resistant populations of bacteria. Once a resistance trait is selected, host bacteria can transfer genes between individuals (horizontal gene transfer) via transferrable genetic elements (e.g., plasmids) creating an enhanced resistome (Wright 2007, 2010). Thus resistance can spread among microorganisms once a gene enters a system, including target organisms that are pathogenic (Dantas and Sommer 2012).

Microorganisms can develop resistance to many environmental factors, including heavy metals, disinfectants, nutrient conditions, and temperature. However, resistance to antibiotics is perhaps that of greatest contemporary concern in society. It has consequences which impede the efficacy of infection control and treatment—with health-related, economic, and societal consequences. It is commonly believed that this type of resistance is only driven by the excessive use of sub-inhibitory concentrations of antibiotics; again, the extent can be argued. While this mechanism

remains the major contributor to antibiotic resistance, it has been recently observed that pressures from environmental pollutants can also provide a level of selection pressure.

Bacterial communities respond genetically to pollutants via evolved mechanisms for their self-protection (Alonso et al. 2001). For instance, metals (or potentially toxic elements) in the environment may contribute to microbial cellular health as a micronutrient, while at elevated levels generating a stress response and resistance development (Beaber et al. 2004; Ashbolt et al. 2013). An example of this response has been observed in the development of copper-resistance mechanisms in bacteria isolated from soil with a high-metal content (Berendonk et al. 2015). Other metals, such as chromium and mercury, have limited biochemical merit and cause oxidative stress. Unfortunately, defence-associated metal resistance genes are often closely associated with those responsible for AMR as both reside on mobile genetic elements.

This co-selection of metal resistance (or other resistance mechanisms, e.g., those against toxic organics or disinfectants) and antibiotic resistance can occur by one of two processes: co-resistance or cross-resistance (Baker-Austin et al. 2006). Co-resistance occurs when selection of one phenotype simultaneously selects for other genes located on the same genetic element. On the other hand, cross-resistance occurs when the antibiotic and metal have similar biochemical pathways or targets in the cell. Consequently, when a resistance response is triggered, the cell defence becomes effective against both metal and antibiotic toxicants. As such, the environment acts both as a reservoir of resistance traits and a bioreactor containing chemical stressors, providing opportunities for genetic exchange. There is, therefore, significant potential for these traits to disseminate to clinically relevant pathogens.

The relationship between metal tolerance (or resistance) and AR has been known; reviews can be found in the literature (e.g., Baker-Austin et al. 2006; Martinez 2009; Seiler and Berendonk 2012; Perry and Wright 2013). However, microorganisms of clinical significance have been found resistant to multiple antimicrobials, including metals, by susceptibility assays (e.g., Marques et al. 1979; Dhakephalkar and Chopade 1994; Bass et al. 1999; Ghosh et al. 2000; Guo et al. 2014), suggesting that a link between genetic traits exists.

In the environment, relationships between metals and AR proliferation were first noticed in highly contaminated areas, including outflows of insufficiently treated wastewater and biosolids (Graham et al. 2011; Knapp et al. 2012; Su et al. 2015), agricultural wastes (Ji et al. 2012; Zhu et al. 2013; Li et al. 2015), industrially contaminated areas (Stepanuskas et al. 2005; Wright et al. 2006; Graham et al. 2011; Knapp et al. 2012; Abella et al. 2015; Hu et al. 2016; Rodgers et al. 2018, 2019, 2020), and direct application via metal exposure experiments (Berg et al. 2005, 2010; Stepanuskas et al. 2006; Knapp et al. 2011). AR presence in these cases has often been indicative of exposure to elevated metal pollution.

Less information exists on less-impacted soils and basal (e.g., pristine natural) levels, but evidence suggests that risks still exist. The geochemical nature of soils, collected in the 1970s for a national archive, had correlations with various antibiotic resistance genes found among their bacterial communities—including those for

tetracyclines, beta lactams, and erythromycin (Knapp et al. 2011). Similar patterns observed in residential soils, all have sub-regulatory levels of metals (Knapp et al. 2017). In some cases, the metal content may not directly correlate with AR genes, but increase the mechanisms (e.g., integrases) by which genes may become horizontally transferred to other bacteria—thus increasing the risk via frequency of potential exchange.

Besides metals, some persistent organic compounds will co-select for antimicrobial (including antibiotic) resistance genes, including pesticides (e.g., Anjum and Krakat 2016), polychlorinated biphenyls (Guidice et al. 2013), and disinfectants (Tandukar et al. 2013; Khan et al. 2016a, b, 2017; Zhang et al. 2016). Additionally, polycyclic aromatic hydrocarbons (PAHs) are ubiquitously found environmental pollutants that have the capability to enhance the abundance of AMR in microbial communities. PAHs are organic compounds with multiple aromatic rings fused in a single compound. PAHs can either be phytogetic—originating from plant materials, petrogenic—from petroleum products or sources, or pyrogenic—resulting from combustion processes. In addition to their potential sources are the distribution and abundance of compounds, and their associated toxicities.

The association of PAHs with AMR has been found in lake-sediment pollution (Máthé et al. 2012), coastal areas (Wang et al. 2017), and soils (Chen et al. 2017). Areas with PAH contamination have been reported to have increased prevalence of genes encoding efflux pumps, detoxifying transporters (Chen et al. 2017), and also conjugative transfer via class I integrons (e.g., Wang et al. 2017).

Since metals and certain PAHs (e.g.) are also widespread in the environment and do not immediately degrade, these compounds can potentially provide a long-term selection pressure. Resistance development is not only due to the presence of high concentration of antimicrobials; rather low concentrations of contaminants, which cause cellular stress to microorganisms, could also provide the selective pressure.

Climate change and AMR represent contemporary topics of discussion. In a recent meeting among the members of Centre for Water, Environment, Sustainability and Public Health (a University of Strathclyde, Department of Civil & Environmental Engineering research group), various cross-disciplinary researchers had a discussion about the possible impacts of climate change on the patterns of antimicrobial resistance. Some of their thoughts are outlined as:

1. Pathogen; their fate, prevalence and gene transfer.
2. Agriculture-related changes.
3. Water distribution and quality.
4. Melting glaciers and permafrost thaws.
5. Hydrological changes and legacy pollution.

Here, we present our thoughts.

10.1 Pathogens

10.1.1 Pathogen Prevalence

At the community scale, changes in precipitation levels and temperatures can be expected to alter the spatial distribution of pathogen vectors. These vectors may be biological (e.g., flies) or non-biological (e.g., dust, fomites) (Nordor et al. 2018).

For example, climate alterations have the potential to alter the range of disease-spreading insects such as the mosquito *Anopheles*, a vector for *Plasmodium*—an obligate parasite of the mosquito. Many *Plasmodium* species cause malaria, with *Plasmodium falciparum* putatively linked to carcinogenesis (Lehrer 2010; Nordor et al. 2018). Elevated CO₂ and changes in air temperature are climate effects with the greatest potential to alter the distribution of malaria via changes in disease vector distribution. Temperature changes will have an indirect impact on soil moisture dynamics, providing a further mechanism to alter the life cycle of malarial vectors. The presence of stagnant water due to increased precipitation rates would also increase the breeding area for the *Anopheles* vector. Therefore, climate change will alter the life cycle of the *Anopheles* vector, along the life cycle of *Plasmodium* itself (Dhimal et al. 2015; Le et al. 2019).

Changes in distribution of malarial areas are anticipated due to climate change, leading to higher malarial burdens (Campbell-Lendrum et al. 2015). Moreover, climate change is expected to impact a range of other vector-borne pathogens in a similar manner. Examples include dengue fever, west Nile virus, tularemia, rabies, chikungunya, and Lyme disease (Green et al. 2008). The principal vector of Lyme disease—the arthropod *Ixodes scapularis*—is anticipated to experience a 213% increase in suitable habitat area within the North American continent by 2080. This effect is anticipated to be driven largely by expansion of viable breeding territory into Canada due to alterations in temperature caused by greenhouse gas emissions and sulphate aerosols (Brownstein et al. 2005).

Climate change will generate changes in daily life, such as increased use of air conditioning systems due to elevated indoor temperatures (Vardoulakis et al. 2015). It has been recognised in the past that indoor environments can harbour microbial communities which vary with geographic location. For example, temperate climate zones harbour far more diverse fungal communities than tropical climate zones (Amend et al. 2010). Significant expansions in the temperate “humid continental climate” (Dfb) are anticipated by 2080, particularly across Russia and parts of India. This would suggest that regions with significant human populations may be exposed to fungal communities of increased diversity due to climate change, with potential impacts on human health.

Heating, ventilation, and air conditioning systems as well as settled dust and outdoor air are well recognised as sources of indoor airborne microorganisms (Prussin and Marr 2015). Airborne fungal particles are of particular concern, as a cause of allergies and even cancers. Climate change may lead to significant effects on global fungal populations, with the spread of thermo-tolerant species being anticipated (Garcia-Solache and Casadevall 2010). These effects may be amplified

in urban areas (McLean et al. 2005). The reduction in the thermal gradient between environment and mammalian hosts generated by climate change is anticipated to increase the range of potential fungal diseases (Garcia-Solache and Casadevall 2010). Any increased use of domestic air circulation systems due to climate change—for either heating or cooling—may become linked to alterations in aerobiology, with subsequent potential impacts on human health (Fernstrom and Goldblatt 2013).

Specific geographic sites for increased fungal diseases have been identified in North America, with the increase in dry summers and increased precipitation late in the year enhancing the spread of *Blastomyces dermatitidis* and *Coccidioides immitis*, both of which are associated with varied health effects, including bone disease (Green et al. 2008).

Within the USA, a 2–4% rise in occurrence of antibiotic resistant bacteria belonging to the genera *Escherichia*, *Klebsiella*, and *Staphylococcus* has been associated with regions of elevated local temperature versus cooler areas (MacFadden et al. 2018). There is a clear link between increased temperature and population density, with increased prevalence of antimicrobial resistance being linked to these elevated temperatures (MacFadden et al. 2018). These effects were observed to be consistent across almost all classes of antibiotics and pathogens, and this association has grown stronger over time. While the selective pressure of antibiotic use is considered to be the largest contributor to the emergence of antibiotic resistance, it has become apparent that climate-change associated factors such as increases in air temperature (Beck et al. 2018) and increased urban density (Güneralp et al. 2017) have potential to increase the prevalence of antimicrobial resistance in many bacterial species relevant to human health.

The negative effects of antimicrobial resistance are ever-increasing due to the uncontrolled use of antimicrobials for the treatment of various infectious diseases. Changing patterns in pathogen distribution are expected to expand the geographic range and intensity of antimicrobial use. For example, the expansion in the viable area of *Ixodes scapularis* into Canada is likely to increase the use of doxycycline and ceftriaxone to combat the causative pathogenic bacterium *Borrelia*. While the emergence of antibiotic resistance has not been observed in *Borrelia* (Sharma et al. 2015), the increased use of doxycycline and other antibiotics such as amoxicillin and even macrolide antibiotics may be associated with increased resistance of other species present in the environment, as observed with *Streptococcus pneumoniae* (Karcic et al. 2015). Similar effects may be anticipated due to increased use of antifungal treatments in response to elevated levels of fungal diseases linked to climate change (Fernstrom and Goldblatt 2013; Prussin and Marr 2015; Vardoulakis et al. 2015), leading to altered geographic distribution of antifungal resistance.

10.1.2 Gene Transfer

HGT (horizontal gene transfer) is a process through which organisms can exchange genetic information without reproduction. This process allows the exchange of

functional genetic material such as virulence, xenobiotic metabolism, and antibiotic resistance genes (ARG). This transfer can occur even at the domain level—such as between bacteria and archaea—and occurs in many different environments, including soil, seawater, and within the human body (Aminov 2011). HGT is linked to emergence of some microbial traits harmful to human health and wellbeing, including antibiotic resistance.

Ecology and environmental conditions have been identified to significantly influence the gene transfer among microorganisms (Fuchsman et al. 2017). Indeed, it is thought that ecology is even more significant in influence than phylogeny (Smillie et al. 2011). This has been evidenced by the high rates of gene transfer between bacteria and archaea in environments, which are conducive to the growth of species from each of these domains. This effect is particularly pronounced in the extremophilic bacteria and archaea, such as thermophiles and halophiles.

Changes in climate are linked with increased salinity in locations such as the Arctic Ocean (Greene and Pershing, 2007), as well as coastal estuaries and aquifers (Titus 1989). These effects may expand the geographic distribution of growth sites suitable for extremophiles, with a concomitant increase in horizontal gene transfer between highly varied species of bacteria and archaea.

In soils, temperature, moisture levels, pH, and soil type have all been associated with changes in rates of conjugal plasmid transfer (Aminov 2011). Changes in soil temperature have been associated with climate change, dependent upon geographic location. For example, warming trends have been observed in the Tibetan Plateau (Fang et al. 2019), Alaska and Siberia (Oelke and Zhang 2004), and Russia (Zhang et al. 2001). There is also potential for climate-change associated soil acidification in a number of environments (Rengel 2011). Associations between climate change and soil moisture are complex, being influenced by changes in precipitation and, therefore, potentially broader climate classification changes (Seneviratne et al. 2010; Beck et al. 2018).

Increasing pH from 4.5 to 8.5 is linked with a general increase in gene transfer rate at 22 °C, with the effect becoming less pronounced at 37 °C (Rochelle et al. 1989). Similarly, increasing temperature from 22 °C to 29 °C is linked to a decrease in gene transfer rates in *Agrobacterium tumefaciens* (Dillen et al. 1997).

In summary, climate change can be expected to increase the levels of HGT in the environment through a range of mechanisms, such as increased sea and soil temperatures, soil acidification, and changes in ocean salinity. Altered microbial community compositions due to climate change effects may also bring previously disparate microbial species into closer contact. Increased levels of HGT have been directly linked to the generation and spread of antibiotic resistance in the environment (Ventola 2015). Therefore, climate-change effects have significant potential to increase the spread of antibiotic resistance genes.

10.2 Agriculture

The occurrence and prevalence of antimicrobial- and drug-resistant organisms and genes have been associated with the selective pressures on the usage of antibiotics in both clinical and agricultural sectors (Levy 1997). Agricultural practices have been considered a major culprit for the increase in antibiotic-resistant strains of bacteria (Silbergeld et al. 2008; Kennedy 2013; John 2014). For instance, in the USA alone, about 13 million kg, or 80% of all antibiotics, has been associated with livestock production annually (Hollis and Ahmed 2013). On a global scale, Van Boeckel et al. (2015) reported that 45–172 mg of antimicrobial agents is consumed annually per kg of animal (e.g., cattle, chicken, and pigs) produced.

10.2.1 AMA and AMR Pathways in Agriculture

Agriculture has been recognised to have many reservoirs/hotspots and pathways involved in the dissemination of AMA (antimicrobial agents) and AMR within the agricultural environment and the food processing industry (Thanner et al. 2016). The general transmission route or pathway is typically from animal (livestock) to animal-derived manure to soil to water and to sediments, with human (farmers) and animals as hosts. Several authors have identified hot spots of ARG (antimicrobial resistance genes) and ARB (antimicrobial resistant bacteria) to include the digestive tract of farm animals and humans, manure, wastewater treatment plants, and the soil or rhizosphere (Zhu et al. 2013; Wu et al. 2014; Woolhouse et al. 2015; Thanner et al. 2016; Manyi-Loh et al. 2018). Other possible water-related hotspots for ARG and ARB include: rivers and lakes, sediments, biofilms in aqua-cultural systems, irrigation systems, slaughterhouses, as well as on plant surfaces (Thanner, et al. 2016). Soil and water tend to function as mixing media or sinks for the mobile genetic elements (MGEs), as well as sources of AMR (Riesenfeld et al. 2004; Xiao et al. 2016).

Antibiotics such as tetracyclines, sulphonamides, lincosamides, aminoglycosides, macrolides, β -lactams, and pleuromutilins with potentially adverse effects are administered to livestock globally for treatment or therapeutic purposes, for sub-therapeutic purposes for growth promotion, as prophylaxis and/or metaphylaxis (Mellon et al. 2001; Apata 2009; Landers et al. 2012; Abou-Raya et al. 2013; Finley et al. 2013; Pham Kim et al. 2013; De Briyne et al. 2014; Baynes et al. 2016; Manyi-Loh et al. 2018). This has led to increase in resistant bacteria within the gut flora of livestock and the deposition of antibiotic residues in products such as meat/muscles/fat, milk, eggs, liver, and kidney available for human consumption (Witte 1998; Aarestrup 1999; Manyi-Loh et al. 2018). Further, animal excretions (urine and faeces) containing antibiotic residues, ARBs, and ARGs may be released into the agricultural environment as raw manure often used for soil fertilisation (Acar and Moulin 2006).

The dissemination and fate of antimicrobials within the agricultural sector depend on:

1. the pattern of administration of the antimicrobials, the metabolic activities and transformation processes within the animal, the potential of releasing the compounds into the environment through animal excrements (European Medicines Agency 2018);
2. their physicochemical properties such as shape, size, molecular structure, solubility, and water repellence (Thanner et al. 2016; European Medicines Agency 2018);
3. environmental effects such as changes in climatic conditions, soil types, erosion, hydrology—surface and groundwater (Carlson and Mabury 2006; Davis et al. 2006; Kuchta et al. 2009; Park and Huwe 2016; Pan and Chu 2017; European Medicines Agency 2018);
4. environmental fate, including sorption properties (Tolls 2001; Lin and Gan 2011; Thanner et al. 2016), abiotic or biotic transformation/degradation processes (Thiele-bruhn and Peters 2007; Reichel et al. 2013; Cui et al. 2014; Manzetti and Ghisi 2014; Duan et al. 2017); and,
5. uptake by crops or pasture (Kumar et al. 2005; Dolliver et al. 2007; Kuchta et al. 2009; Carter et al. 2014).

Soil acts as a natural reservoir for AMA and ARBs since a wide range of known and unknown (or uncultured) AMR determinants have been detected in non-fertilised soils (Riesenfeld et al. 2004; Maron et al. 2013; Marti et al. 2013; You and Silbergeld 2014; Xiao et al. 2016). However, antimicrobial agents are mostly introduced to soil via fertilisation with raw manure collected from animal sources treated with antimicrobials, bringing metabolites of AMA and microbes with ARG existing on mobile genetic elements (MGE) (Hamscher et al. 2005; Binh et al. 2008; Zhu et al. 2013; Wolters et al. 2015; Thanner et al. 2016). Additionally, AMAs are added through the use of irrigation with wastewater and treatment of crop diseases with antibiotics (Finley et al. 2013; Oluyeye et al. 2015). Depending on soil temperature, pH, nutrients, and oxygen concentration as well as microbial diversity, ARG may be transferred to soil microbes through HGT (i.e., via conjugation, transduction, and transformation mechanisms), resulting in enrichment of taxa and decline in the population of organisms significant for soil quality (van Elsas and Bailey 2002; Aminov 2011; Perry and Wright 2013; Ding et al. 2014; Fahrenfeld et al. 2014; Jechalke et al. 2014; Forsberg et al. 2015). According to the European Medicines Agency (2018), there may be a positive correlation between the factors that promote the persistence of a compound in soil and factors that enhance their potential to select for resistance within the same microbiome. It has been reported that an increase in soil moisture content from 15% to 25% led to a decrease in the half-life of an antibiotic (sulfadimethoxine) from 10.4 to 4.9 days (Wang et al. 2006), while a similar increase in temperature resulted in the degradation of norfloxacin (Yang et al. 2012). In contrast, other studies have found that warmer temperatures (30–45 °C) could enhance the antimicrobial effects and antibiotic resistance of common pathogens and bacterial biofilms (Rachid et al. 2000; Hajdu et al. 2010; MacFadden et al. 2018).

The aquatic environment also serves as source and sink of antibiotic-resistant bacteria and resistance genes (Biyela et al. 2004; Baquero et al. 2008). Also, antimicrobial agents (or mobile resistant genes) in raw manure can be translocated via the action of rainfall runoff and/or soil erosion from the surface of fertilised soils to nearby surface or groundwater bodies, depending on the properties of the AMAs, the soil, and hydrological effects (Pollard and Morra 2018). Although studies on the mobility and transport of antimicrobials in the environment are scarce, the European Medicines Agency (2018) suggests that these behaviours will vary considerably for different antibiotics.

Humans, especially those involved in agriculture (e.g., farmers) typically become hosts to commensal organisms and resistant pathogens via ingestion. Farmers and their families can transmit AMAs to livestock through contact, since the human skin and digestive tract serve as reservoir for some of these pathogens (Acar and Moulin 2006). However, this route of transmission depends on several factors including geographical location or region, farming system adopted, size of farm, hygiene, ethno-cultural and religious practices (Lozano et al. 2016).

10.2.2 Influence of Climate Change on Agriculture

Climate change will directly impact agricultural climate resources (such as precipitation and temperature) and cause changes in livestock productivity, crop/plant community composition and productivity, soil microbial communities, and the general agro-related ecosystem, as well as surface and groundwater hydrology (Kim et al. 2010; Bardgett et al. 2013). It has been predicted that climate change will result in further reduced agricultural productivity in regions with hitherto low agricultural productivity levels (Harvey et al. 2014). Some studies report that changes in the amount and quality of feed as well as increased heat stress may result in a 25% decrease in animal production (van de Steeg and Tibbo 2012; Lewis, et al. 2018) with higher temperatures leading to lower daily milk yield (Verner 2012).

10.2.3 Possible Changes Induced by Climate Change on AMR in Agriculture

Thanner et al. (2016) provide a comprehensive list of knowledge gaps in AMR in agriculture, justifying the difficulty to reach valid conclusions on the prediction of key factors, like climate change, on AMR prevalence in the agricultural sector. The discussions in the aforementioned sections also show that for the few available studies, there are contradictions in findings regarding the behaviour of AMA/ARG under variable climatic conditions. It has been suggested that global-scale surveillance programmes utilising comparable test methods may be necessary to provide data on areas like the occurrence/abundance, transfer pathways, and factors influencing the selection, spread, and persistence of AMAs/AMR in the different compartments of agriculture, and the environment in general (Thanner et al. 2016;

Manyi-Loh et al. 2018). This will contribute towards better understanding, prediction, and management of AMR in agriculture.

Nevertheless, the socio-economic trends induced by climate change are expected to influence land use patterns (Karmakar et al. 2016) and general agricultural practices, with possible indirect impacts on AMR. The Food and Agriculture Organization of the United Nations (2016) predicts that climate shocks may lead to economic downturn for farmers, especially small-scale farmers, as productive capital or assets may be sold to absorb the shock. In several countries in the Near East and North Africa region, extreme droughts and climatic events could result in crop failure and lead to food insecurity, malnutrition, famine, and starvation (Elasha 2010; WFP and ODI 2015). These factors coupled with the growing population imply that there would be greater demands for food (including animal proteins) across the world, thereby placing pressure on agricultural production (Padol et al. 2015). The tendency to use antibiotics to promote animal growth will become almost inevitable especially in developing countries. Currently, the factors influencing the usage of antibiotics vary considerably across regions and countries (World Health Organisation 2012). These factors include: land use, sources of contaminated water, animal demography as well as national and international trade and policies (World Health Organisation 2012). Antimicrobials that have been banned in several countries, including developed countries, are still being used in developing countries (Moyane et al. 2013; Adebowale and Adeyemo 2016). It has also been predicted that to meet increasing consumer demands, the use of antibiotics in Brazil, Russia, India, China, and South Africa (known as the BRICS countries) is expected to double (Van Boeckel et al. 2015). China is reported to be the highest producer and user of antibiotics for humans and animals (Manyi-Loh et al. 2018). A study by Lee et al. (2001) has predicted that, in the future, a significant percentage of animal-derived proteins packaged as food for human consumption would have received some sort of chemotherapeutic or a prophylactic agent.

10.3 Water Distribution and Quality

10.3.1 Surface Waters

Drought and flood are two extreme conditions, resulting from climate change that can dramatically affect the water quality, having significant effects on concentration of metals, organic pollutants, and pathogenic bacteria (Xia et al. 2015). The increase in the world average temperature could have greater impact on world's water resources and decrease the availability of freshwater resources. There are many direct and indirect effects that could have lasting impacts: (1) re-distribution of water and its availability as a source of drinking water; (2) changes to the water quality as driven by increased biochemical activities; (3) changes in the fate and presence of pathogens likely involved in the AMR process; and (4) impacts on treatability of water, all of which could impact the risks associated with AMR.

Climate change is a major contributing factor in the disruption of water cycle and water supply systems (de Oliveira et al. 2015), and these strongly relate to elevated temperature (Xia et al. 2015). Increased temperatures accelerate evaporation and transpiration leading to water loss from soil and plants (Bates et al. 2008). Many water-supply systems face water scarcity and reduced water quality, and climate change is considered as one of the reasons for this shortage of water (Delpla et al. 2009).

Climate change deteriorates water quality (Xia et al. 2015) by different biochemical processes (Delpla et al. 2009). As we know, microorganisms support the existence of life on the earth, and climate changes depend on the response of the microorganisms to the environment (Cavicchioli et al. 2019), including their key role in different nutrient cycles (Azam and Malfatti 2007). These biochemical and microbiological reactions are temperature dependent (Whitehead et al. 2009); for example, higher temperatures reduce the concentration of dissolved oxygen in water. Anoxia, as we already know in eutrophic systems, leads to further changes in water quality, such as the further release of nutrients and metals. This cascades to increased rates of nutrient assimilation and biomass production—including algal blooms and anoxic dead-zones (de Oliveira et al. 2015). However, long-lasting results may not be clear; while immediate-nutrient effects are observable, studies show that climate change (i.e., increasing temperatures) may decrease nutrient concentrations in surface river waters (Alam et al. 2013; Hosseini et al. 2017), caused by cumulative assimilation by biota.

Anthropogenic activities tend to have a direct effect on water pollution while climate change can have indirect effects on decrease in water quality in supply system (Bates et al. 2008). Water temperatures have dramatic impacts on its treatability for drinking water and may require further treatments to maintain the potability. Increased water temperatures have the unfortunate consequence of requiring higher dosages of chemical disinfectants (e.g., chlorine), and they also result in increased formation of disinfectant by-products after disinfectant treatment—e.g., the formation of chloroform from chloramine-treated water after 3 days at higher temperature (Yang et al. 2007). This not only affects the potability of drinking water, but also the increased disinfectant chemical loadings can impact the microbiome.

10.3.2 Water Distribution

The obvious, but highly unfortunate consequence is that alterations in water availability will lead to the re-distribution of populations, but it will also encourage the use of waters with reduced quality to meet demand. Thus requiring additional treatment and/or distribution of water.

Water distribution systems are complex systems. They often represent environments with low concentrations of antimicrobials, e.g., chemical disinfectants, to maintain the level of assurance that the water remains potable. Chemical disinfectants, like the antibiotic therapies, are designed to exhibit either biocidal or biostatic effects on the bacteria. At elevated concentrations, they may be quite

effective. But, disinfectant concentrations and efficacy decline with temperature and deterioration of water quality (e.g., chlorine demand). At some point along the distribution system, or in time, the concentrations could decline to “sub-lethal levels”. Instead of inhibition, we could see population selection. Any surviving bacteria would have undergone selective pressures for resistance traits that contribute to their survival. This could be resistance traits against the disinfectant, but also other chemicals present, including those associated with poor water quality—e.g., metals.

Even if bacteria could be removed at the point of treatment, distribution systems still have the risk to become colonised by pathogens having antimicrobial resistance due to limitations in treatment technologies and leakage; this becomes a mechanism and source, by which resistant infections to human beings could result (Buse et al. 2012). This could be further exacerbated by the prolonged storage of water in (e.g.) building cisterns (Falkinham et al. 2015), where disinfection efficacy declines and the opportunity for contamination increases. Thus, water supply systems could represent an unsuspecting source of AMR, which could become worsen by declining availability, deteriorating water conditions, and challenged treatment efficacy. As such, there is a risk of spreading of antibiotic resistant bacteria to human populations via insufficiently treated drinking water (West et al. 2011).

A number of antibiotic resistant genes including *tet*, *sul*, *van*, and *amp* have been reported being transported via water bodies, and have been found in treatment plants and distribution systems (Schwartz et al. 2003; Pruden et al. 2006; Prado et al. 2008; Czekalski et al. 2012; Guo et al. 2014; Bergeron et al. 2015; Adesoji et al. 2016). The bacteria with antimicrobial resistance are not easy to treat (Levy 2002) and pose a potential health risk for the immune-compromised population (Lee et al. 2010). Due to their impacts on human health, antibiotic resistance has been announced as global health emergency (Sanderson et al. 2018), and there is an urgent need to minimise the environmental pollution due to antibiotics (Singer et al. 2016). Although the use of antibiotics has been reduced in different parts of the world, the problem is not diminishing as their resistance is widely spread among different environments. World Health Organization has started a global action plan to eradicate the problem through public awareness and sustainable investment (WHO 2015; Singer et al. 2016). Distribution systems and the complex interactions of source water availability, conditions, and treatment exemplify the challenges ahead.

10.4 Melting Glaciers and Permafrost Thaws

Warming climate in glacial areas causes huge physical ($\Delta\sigma > 2000$ MPa), chemical, and biological stress to surface and near surface environments. Ice sheets had once wide coverage during the Pleistocene (~2.5 Ma to ~12 ka) reaching ~40 °N in North America. Currently, glaciers and continental ice-sheets cover ~10% of the land; permafrost currently covers ~23.9% (Zhang et al. 2008) of exposed Northern Hemisphere land surface. The glacial cycle produces large vertical and flexural stress changes to the lithosphere (Lemieux et al. 2008). Glacial retreat results in

hydromechanical changes: isostasy, permafrost melting, ice sheet un-loading, groundwater flow/chemistry, and pore fluid pressure. Deglaciation removes vertical, flexural, and hydraulic loads from the lithosphere. Lithospheric rebound occurs, pore fluid pressures change (Neuzil 2012) in response to the changes in stress. High-pressure heads during glacial advance cause groundwater to migrate from the surface to depth (Lemieux et al. 2008). When the hydrostatic pressure of ice sheet is removed, exfiltration of deep saline brines occurs. Fresh glacial groundwater becomes input to the groundwater system.

Groundwater chemical conditions and subsurface flow pathways change during the glacial cycle, having the potential to mobilise and transport: brines, heavy metals, and organics at the surface. Studies of the Laurentide ice sheet, during the Wisconsin and Pleistocene glaciations in North America show brine formation and migration causes changes to ground and surface water chemistry across a glacial cycle. Brine rich in sodium chloride formed from sea water during cold glacial periods under permafrost through a process of cryogenic brine formation. Cryogenic brines form when water freezes (Starinsky and Katz 2003), solutes are not stored in the ice and concentrate in the remaining water. Cryogenic brines form alongside permafrost (McIntosh et al. 2011) in the near surface. During static glacial periods brines and mineralised halite remain stable in the subsurface. Warm periods result in permafrost thawing and glacial melt; this results in the up-welling of saline brines (Starinsky and Katz 2003), which can then reach the surface and soil zone. Deglaciation has the largest chemical impact on groundwater: saline brines are driven to shallower depths. Melt water infiltrates and dissolves halite minerals (deposited during permafrost formation in glacial periods). Infiltrating melt water triggers microbial mediated methanogenesis (McIntosh and Walter 2005). The effect of glacial cycles results in large swings in the surface and soil water chemical conditions.

Conditions in the permafrost differ; Siberian permafrost has high methane and negative redox potential (Willerslev et al. 2004) indicating a harsh anaerobic condition. Antarctic permafrost has high redox potential and alkaline pH compared with neutral pH in Siberian sites. Thawing of permafrost is documented to release CO₂ as well as methane into the atmosphere (Hodgkins et al. 2014). However, during the thawing process CO₂ and CH₄ gases will also get dissolved into the melt water. This in turn will lead to lowering of pH in thawed permafrost. As permafrost thawing rate increases over time (Haldorsen et al. 2010), melt water surrounding patches of permafrost promote further thawing. Release of organic matter and methanogenesis CH₄/CO₂ production will increase exponentially as permafrost thawing rate increases. Increasingly rapid changes to the soil environment will cause stresses to the microbiome as a consequence of the changing climate. Previously trapped and accumulated organic matter in permafrost (Turetsky et al. 2000) is released into the water system during thawing. The increase in organic matter (OM) input from melting permafrost supplies the OM source used in methanogenesis. OM input from melting permafrost includes primary and secondary metabolites which are biologically available and can be directly up taken by plants and microbes.

Melting permafrost, in response to warming climate, releases major ions making them available in the soil zone. Release of major ions increases their concentration in

fresh surface water environment affecting aquatic ecosystems. Both major ions (Ca^{2+} , Mg^{2+} , SO_4^{2-} , NO_3^-) and trace elements (e.g., Ni, Hg, Pb, Cr, As) increase with increased melting of permafrost. Release of toxic trace metals into freshwater environments can have wide reaching impacts on the ecosystem. Increased nitrate, phosphate, and sulphate are made available in melting permafrost. High nutrient input and rapid fluctuations stress the aquatic ecosystem. Rapid changes in toxic trace elements and nutrients into the environment will cause shifts in the microbiome, and the trace organics and metal may impact the resistome—or presence of the resistance genes (Colombo et al. 2018).

There are evidences for the release of heavy metals and the consequential presence of AMR (particularly metal). For example, strains of bacteria from permafrost soil samples in China show Pb resistance and Pb^{2+} biosorption (Li et al. 2017). Environmental strains of *Acinetobacter lwoffii* from permafrost contain genes for heavy metal resistance (including Cr, As, Hg, Cu, Ni, Co, Zn); the chromosomal resistance genes were homologous to plasmid genes found in *A. lwoffii* (Mindlin et al. 2016). Mercury resistant bacteria were discovered in permafrost near Kolyma, Canada (Petrova et al. 2002).

While it is expected to have associated resistance traits to elevated metal concentrations, there have been evidences of expanded spectrums. Viable bacteria found in Siberian permafrost showed antibiotic and heavy metal resistance. Resistance is thought to be developed because of the harsh conditions (constant freezing, poor nutrient availability, inorganic and organic inhibitors) the strong selection pressure (Zhang et al. 2013).

Microbes trapped in permafrost have been shown to have antibiotic resistance genes similar to modern day bacteria (D'Costa et al. 2011). Thawing ground ice and sediments can release ancient resistant bacteria to the surface environment. There is little evidence to show that increased organic matter is transported to aquatic environments, it instead likely remains in the soil and saturated zones.

10.5 Hydrological Changes and Legacy Pollution

Increased industrial activity in society is an inevitable and on-going process. With a growing demand for goods and services, pristine and rural landscapes have become transformed into urban centres with increased population densities, factories, and manufacturing. Other areas become exploited for natural resources (e.g., mining) and exploration and/or generation of energy (e.g., oil and gas industries). Many European and North American countries have experienced this Industrial Revolution during the eighteenth century; many other countries throughout the world have recently undergone, or undergoing, their own versions of revolution. Whilst development of industries and the technology became a period of societal advancement, it was also inevitably the era of pollution, where by-products of anthropogenic activities and industry were released into the surrounding environment (Krishna and Govil 2007; Reza et al. 2010) and became entrained into the soil and sediment layers as legacy pollutants.

These legacy pollutants include a variety of potentially toxic elements (e.g., Pb, Cu, Cr, Co, Ni, V, and Zn), polycyclic aromatic hydrocarbons (Rodgers et al. 2019), and bacteria which have been released into sediments due to anthropogenic pollution (Krishna and Govil 2007). Often, these contaminants that remain in the environment are rather recalcitrant, meaning either they do not degrade or do so very slowly. Evidences have been found in recent studies, for instance, (Rodgers et al. 2018, 2019, 2020) in the Clyde estuary (UK) highlight that a higher legacy of anthropogenic activity can be found in sediments from historical industrialisation. PCA was used in this study to distinguish between natural and anthropogenic contaminants to identify sites with high industrial depositions. Results indicate high levels of heavy metals and PAHs present near heavily used industrial sites of the estuary, several of which being pollution “hotspots”, indicating pollutants have accumulated over time. Sediment quality were greatly diminished due to these inputs, and alterations in alkalinity and tides have had little to no impact on the concentrations of PTEs present (Rodgers et al. 2019).

Climate change can result in changes in the hydrological cycles, leading to consequential changes in precipitation, water flow, and ultimately erosion of soils or scouring of sediments (Krishna and Govil 2007). Pollutants, for example, in the sediment layers could increasingly become re-entrained into advective flows, becoming re-distributed downstream creating an additional pressures on environmental and public health.

There is not much evidence of risk with antimicrobial resistance resulting from changes in hydrology, but the extent of their presence in the environment and their relation to pollution has become increasingly known over the last few decades. The relationship between environmental conditions and the development and dissemination do apply; the risks could be hidden. We can postulate some scenarios where this may become problematic:

1. Polluted soils and sediments become a bioreactor for bacteria, subsequently enriching resistance traits. Post-industrial sediments, as mentioned previously, are carriers of adsorbed chemical pollutants that provide additional stress to the microorganisms. The prolonged degradation and retarded release of the pollutant could provide a concentration gradient of exposure, which could provide a wide range of stress conditions, and varied bacterial responses. Populations in situ can either become selected for resistance traits (via chemical toxicity), genetically modified (via increased mutation and genetic selection), or experience increased horizontal genetic transfer.
2. Entombed in polluted sediments, the bacteria could be co-present at the time. When reviewing the period of industrial revolution (in the UK), it was also the period of poor sanitation and wastewater treatment. Sewage and bacteria were discharged into major waterways that were also major industrial centre. In this case, pathogens associated with human or agricultural disease are present in elevated numbers, and could likewise experience the pollution stress. They then become stored, remaining dormant, in sediment layers with their fully developed resistome.

Resulting from either scenario, polluted sediments, harbouring highly multi-drug resistant and potentially pathogenic micro-organisms, become re-introduced into flowing water (Allen et al. 1977). This creates a biological risk to agricultural, aqua-cultural, and human health downstream, as many industries are located on rivers and estuaries due to their necessity for a water source.

The best evidence for this is a recent examination of the Clyde estuary where researchers found chemical pollutant profiles in sediment (30–50 cm depths) that corresponded to past pollutant events, especially in terms of zinc, copper, and arsenic (Rodgers et al. 2020). Examining the extracted DNA from the microbial communities obtained from slices of the sediment cores, there was a corresponding elevation of antibiotic resistance genes for: aminoglycosides, beta-lactams, FCA (fluoroquinolone, quinolone, chloramphenicol, florfenicol and amphenicol resistance genes), MLSB (macrolide, lincosamide, streptogramin B), tetracycline, vancomycin, sulphonamide, and efflux pumps; additionally, genes associated with transposons and integrons, which represent genetic transfer elements, were also increased (Rodgers et al. 2018). Additionally, Tonner et al. (2017) successfully recovered viable isolates from the deep sediment layers, consisting mostly of aquaculture pathogens: *Pseudomonas* spp. and *Aeromonas* spp. resistant to several heavy metals (e.g., Zn, Cu, Cr) and antibiotics (e.g., many beta lactams).

Hydrology in this context refers to the nature of waterways (i.e., rivers, channels, tributaries, and estuaries) and their natural flow pattern or regime near areas of industrial legacy. Many of these areas, which have the continuous stress of variation in salinity and pH's, have been exposed to a myriad of pollutant effluents affecting, one way or another, the presence of bacterial pathogens and the character of their resistome.

Unfortunately, variations in the flow of waterways can become influenced by alteration of the surrounding environment which can be triggered by climate change. The alterations can disrupt soils and sediments and cause potentially pathogenic bacteria to be re-introduced into in-stream processes. This leads to a decrease in the quality of the water in nearby sources such as estuaries subsequently posing a potential threat to human health. In summation, it is important to evaluate the health risks of post-industrial soils and waterways and their potential risk to human life. The hazards of bacteria, which have developed from industrial legacies, are yet to be fully understood.

10.6 Summary

Climate change represents a shift in the balance, and the outcomes and links are complex—and rather difficult to predict. It can only be best speculated based on the indirect results by the changes in the factors that may contribute to the development and dissemination of resistance traits; changes in the chemical composition of the environment that may create additional stress on the microorganisms (e.g., metals and polycyclic aromatic hydrocarbons); changes in the character of the soils and water; changes in human behaviour (e.g., agriculture) and distribution; or the

distribution of pathogens. One common theme that may mitigate the impact of AMR would be (and currently is) the reduction of environmental stress. Further research is needed to understand the microbiome, the resistome, and the impact shifting environmental (e.g., chemical and temperature) stressors—these approaches could be applied to agricultural wastes and soils, wastewater treatment, pathogens discharged into the environment, and the evolution and dissemination upon exposure to ecological stress.

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