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Climate change and antibiotic resistance: a deadly combination

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***Abstract*:** Climate change is driven primarily by humanity's use of fossil fuels and the resultant greenhouse gases from their combustion. The effects of climate change on human health are myriad and becomingly increasingly severe as the pace of climate change accelerates. One relatively underreported intersection between health and climate change is that of infections, particularly antibiotic-resistant infections. In this perspective review, the aspects of climate change that have already, will, and could possibly impact the proliferation and dissemination of antibiotic resistance are discussed.

Keywords: Climate change, antibiotic resistance, antimicrobial resistance

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Introduction

The world is in the midst of an anthropogenic climate crisis, with implications for the survival of humanity and millions of other species of life on Earth. Climate change is directly linked to human morbidity and mortality, and healthcare itself has a large carbon footprint which urgently needs to be corrected.[1–3] However, the primary drivers of climate change are greenhouse gas emissions from fossil fuel use. In addition to being an issue of human health, climate change is an issue of social justice, with marginalized groups at highest risk of experiencing the negative effects of climate change while contributing a relative paucity of greenhouse gas emissions (the wealthiest 10% of the population are responsible for 52% of all carbon emissions).[4]

Regardless of its etiology, climate change has already and will continue to affect human health, likely in increasingly drastic and severe ways.[5] Examples of the effects of climate change on human health include heat-related mortality, food insecurity and reduced crop yields, increased suitability for infectious diseases transmission, rising sea levels, cardiovascular morbidity, mortality from increasingly severe wildfires, and the myriad health effects resulting from other extreme weather events such as floods and droughts.[5] These changes will be felt hardest by marginalized groups, including those in low- and middle-income countries and persons from non-White racial backgrounds and/or with low socioeconomic status, that is, climate change is a social justice issue.[5]

One of the essential pillars that holds up the functionality of our current healthcare system is the availability of effective antibiotics for bacterial infections. Without effective antibiotics, surgeries, cancer treatment, organ transplantation, and community-acquired infections could be fatal, resulting in millions of additional lives lost annually. In addition, some of the gains in childhood survival because of antibiotic availability of effective antibiotics for respiratory infections would be washed away. With the changing climate, this situation will be pushed closer to a breaking point because, as we will demonstrate, climate change and antibiotic resistance are intimately linked. This paper will discuss observations of some of these phenomena already occurring, those that are likely to occur, and those that are possible as the *status quo* maintainers of the world continue to fail to rise to the challenge of climate change.

Heat and antibiotic resistance

Temperature is intimately linked with bacterial processes and infections.[6] Horizontal gene transfer, a major mechanism for the acquisition of antibiotic resistance, is increased by increasing temperatures. In addition, increases in temperature generally increase bacterial growth rates.[7]

There is significant evidence that bacterial infection rates are associated with increases in temperature, a discussion of which follows. An international study of 22 cities found that distance from the equator and socioeconomic factors were both associated with risk of Gram-negative bacteremia.[8] Fewer antibiotic-susceptible *Acinetobacter* infections occur during winter months.[9] Another study found that humidity, monthly precipitation, and temperature were all correlated with rates of Gram-negative bloodstream infections in hospitalized patients.[10]

For the diagnosis of cellulitis, a dose–response relationship between incidence and temperature has been found.[11] Similarly, there was a dose–response relationship between hospital admissions due to urinary tract infections and temperature.[12] The relationship between temperature and infection rate holds true also for surgical site infections after knee and hip arthroplasty,[13] Legionnaire's disease,[14] and other types of surgical site infections.[15]

Not only are infection rates increased by temperature, antibiotic resistance is associated with increased temperatures. Increasing local temperature and population density both lead to increased rates of antibiotic resistance.[16] The relationship between temperature and population density was true for the ubiquitous pathogens *Escherichia coli, Klebsiella pneumoniae*, and *Staphylococcus aureus.*[16] MacFadden *et al.* found that the increases in antibiotic resistance were associated with average minimum temperature,[16] a value which has been on the rise due to climate change.[17] The combination of increased numbers of infections and increasingly antibiotic-resistant pathogens will inevitably lead to more and more antibiotic-resistant pathogens as climate change worsens.

Now we move to one of the most important diarrheal pathogens globally, *Salmonella.* Heat and humidity both increase rates of salmonellosis,[18] which is becoming increasingly antibiotic resistant. In addition, poultry intestinal colonization by *Salmonella* is increased by heat stress.[19] With millions of global cases, the combination of increased case numbers, increased colonization rates in animals, and increasing antibiotic resistance, climate change has the potential to increase significantly the burden and morbidity from salmonellosis worldwide.

Another underexplored consequence of higher temperatures is the effect it will have on human behavior, including prescribers, as higher temperatures increase irritability and reduce critical thinking.[20,21] Telemedicine, increasingly used for all types of medical encounters because of the COVID-19 pandemic, has been associated with increased unnecessary antibiotic prescriptions (visits unrelated to the COVID-19 pandemic), which may be a result of time pressure as visits are shorter when antibiotics are prescribed and patients are more satisfied.[22,23] As increased use of unnecessary antibiotics and local prescribing practices are known risk factors for antibiotic resistance,[16] the association between temperature and behavior could have significant ramifications.

Disasters and infections

As the climate warms, the capacity of the atmosphere to hold water increases exponentially, meaning storms will be more severe and come with more precipitation. More precipitation leads to flooding, flood-related infections, population displacement, refugees, and overcrowding. Overcrowding is associated with increases in infection rates.[24–27] Flooding can result in the spread of waterborne infections because of the overflowing of contaminated water from sewage lines or contamination by livestock.

Nitrogen fertilizers increase antibiotic resistance[28] and therefore, floodwater pollution by nitrogen fertilizers during severe flooding due to climate change will increase antibiotic resistance. Eutrophication, which can be worsened by flooding, increases antibiotic resistance and can lead to dissemination of resistant pathogens and antibiotic-resistance genes.[29]

Extreme weather events resulting in flooding will more strongly disrupt weak sanitation infrastructure, increase crowding in already crowded areas, and spread antibiotic resistance from dissemination of sewage, a known reservoir for antibiotic-resistance genes.[30] With dissemination of antibiotic resistance, progressive use of broad-spectrum antibiotics will be required, resulting in a fatal cycle of the promotion of antibiotic resistance and its spread.

Pollution and antibiotic resistance

More and more intense precipitation will lead to increased runoff and inevitably higher levels of pollution in our water. Pollutants are known to induce expression of antibiotic-resistance genes and bacterial mutagenesis.[31] Increased agricultural runoff (i.e. eutrophication from fertilizers) will increase bacterial blooms in water systems and high concentrations of bacteria will increase opportunities for transfer of antibiotic-resistance genes.

Pollutants, including heavy metals from manufacturing and industrial practices, can be disseminated into the environment with flooding,[32] which will become more severe with the extreme weather events precipitated by climate change. As metals in soil are known to increase antibiotic resistance,[33,34] this process will result in the dissemination of antibiotic resistance.

Antibiotic resistance, waterborne infections, and sanitation

In addition to flooding discussed above, extreme weather events will lead to drought in some areas. Water scarcity during droughts leads to reductions in sanitation and higher densities of people sharing the same water source.[35] With crowding and shared water, waterborne infections are primed for explosive outbreaks. Water and food scarcity run hand in hand, which could result in poorer nutrition on top of increased diarrheal diseases. Children's risk of acquiring antibiotic-resistant enteric pathogens is affected by malnutrition, crowding, and poor sanitation.[36] Inevitably this will lead to more severe diarrhea and higher mortality rates, particularly with higher rates of antibiotic resistance preventing the administration of effective therapy.

Microplastics increase gene exchange in bacteria[37] in water sources, which could lead to increased dissemination of antibiotic resistance. As the climate warms, one can envision a nightmare scenario in which *Vibrio* species increase in prevalence and range due to oceanic warming,[38] become more antibiotic resistant due to microplastics, and lead to outbreaks of antibiotic-resistant cholera and necrotizing fasciitis.

Downstream (indirect) antibiotic resistance

As the climate changes, bacterial and viral infections will be impacted (Table 1). Vector habitats will expand, leading to increased numbers of vector-borne infections.[5] Higher temperatures also increase insect vector activity.[39] Drought leads to elimination of mosquito predators, allowing them to multiply unhindered in the residual pools of stagnant water.[40] With exposure of previously naïve populations, there will be increases in the number of hospital admissions from vector-borne diseases.[5] The result of increased hospitalizations, particularly for those with severe illness requiring intensive care, will be more days with invasive devices and hospital-acquired infections, which are often antibiotic resistant.[41] In addition, patients with critical illness are more likely to be discharged to nursing homes or rehabilitation facilities, which are breeding grounds for antibiotic resistance. Increased throughput through this pathway (i.e. from vector-borne diseases) could result in more antibiotic-resistant infections. The population at risk for vector-borne diseases as a result of climate change is only expected to increase, with estimates of 500 million more people at risk by 2050.[42]

As the range of malaria vectors increases, more persons will acquire the infection, again in persons who are previously naïve and have a higher chance of severe infections (and downstream hospital-acquired infections). With expanding vector range, the areas where antimalarial resistance has been relatively contained will extend and spread, increasing the global burden of antimalarial agent resistance. In malaria-endemic areas with greater than average rainfall due to climate change, there may be increased opportunities for mosquito proliferation due to increased standing water.[5] Climate change has already resulted in the spread of malaria to places previously not endemic.[43]

Another form of antimicrobial resistance related to climate change that is worth mentioning is tuberculosis. Crowding increases transmission rates of tuberculosis[44] and with climate refugees and increased population density/crowding inevitably there will be increased spread of antibiotic-resistant tuberculosis. The co-occurrence of poverty, antibiotic-resistant tuberculosis, and

Table 1. Climate change sequelae and their effects on bacterial and viral infections.

Climate change factor	Bacterial infections	Viral infections
Extreme weather events	+[5]	+[5]
Increased global temperature	+[5,8,10–16,18]	+[5]
Droughts	+[5]	+[40]
Floods	+[29]	+/–
Vector transmission	n/a	+[5]
Vector range	n/a	+[5]

lack of access to medical care and diagnostics could potentially result in a huge outbreak of antibiotic-resistant tuberculosis. Regarding antibiotic-resistant tuberculosis, one study found that reduced humidity (which could occur in areas affected by climate-induced drought), had higher rates of antibiotic-resistant tuberculosis.[45] In addition to aiding the spread of tuberculosis, population density is associated with antibiotic resistance in other organisms.[46]

As a result of climate change, some areas will have more rainfall, whereas others will have more drought, and with drought, wildfires. In addition to human casualties and the loss of biodiversity from massive wildfires, respiratory problems will occur in survivors. A substantial body of evidence demonstrates that particulate counts result in increased cardiovascular morbidity and mortality both in the short term and the long term.[47–49] In addition, direct exposure to fire can result in permanent lung-scarring and lead to bronchiectasis.[50] Patients with bronchiectasis are known to harbor antibiotic-resistant infections bacteria[51] and to have multiple infections/exacerbations, another tributary to the common final pathway linking climate change with antibiotic resistance.

As climate change creates a resource bottleneck, farming and livestock producers will be increasingly pressured to maximize their crop and animal yields. In the past, this has often been achieved with antibiotics. Though by no means is unnecessary antibiotic use in farming/livestock a thing of the past, pressured resources could cause resurgence and increase dissemination of antibiotic resistance within ecosystems.

Lastly, to touch on the COVID-19 pandemic. Climate change increasingly brings humans and animals into contact and has and will continue to result in outbreaks of zoonotic and vector-borne diseases with pandemic potential. With the pandemic, we have seen shortages of personal protective equipment and resultant increases in hospital-acquired infections.[52] As diseases continue to emerge and potentially overlap, these shortages and resultant increases in hospital-acquired infections (which tend to be antibiotic resistant) will only increase. As to the effects of climate on COVID-19 outcomes, the data are mixed, with some studies showing effects of temperature on mortality and others finding no association.[53–56] However, climate change, with its concomitant extreme weather events and particulate matter pollution, contributes to cardiopulmonary morbidity, a known risk factor for poor COVID-19 outcomes. Regardless of the nature of the interaction, because of its ubiquity, climate change is likely to affect the COVID-19 pandemic and its victims.

Conclusion

Climate change is a social justice issue and its unmitigated progression will disproportionately affect the health and well-being of persons in low- and middle-income countries across the globe. In this time, we must take action at every level to reverse the tide of impending climate disaster. There is no fitness cost to bacteria of being antibiotic resistant,[57] and therefore, we must prevent antibiotic resistance due to climate change now, rather than try to fix it later. Antibiotic resistance and climate change are intimately linked and as a profession we have a duty to address both to protect the health of our patients and our planet.

Conflict of interest statement

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