Key Factors in Antibiotic Resistance

Sir,

Antibiotic resistance (AR) continues to be a public health concern that affects close to 2 million Americans each year.[1,2] In comparison to other nations, the United States is one among the highest consumers of broad-spectrum antibiotics with a minimum of 4.3 defined daily doses per person. When we consider the cumulative antibiotic dosage, it is approximately 10–20 daily doses per person.[3,4] Despite regulations regarding the antibiotic usage, we seem to be consuming antibiotics at an astounding rate. We know that continued prescribing of antibiotics increases the development of infections due to resistant pathogens. While your paper touched on the factors that need to be addressed in developing countries, we would like to mention factors that developed nations with high rates of AR should be addressed.

Increased Antibiotics Research

Recently, the United States had a shortage of penicillin G, an essential medication as listed by the World Health Organization.[5,6] While this deficit is resolved due to the increased production at the request of the Food and Drug Administration (FDA), such a shortage of an essential medication should not have occurred in the first place. This medication deficit was due to fewer pharmaceutical companies producing penicillin. Many pharmaceutical corporations no longer research and manufacture antibiotics due to a narrow profit margin.[7] Currently, only four major companies still have a designated "antibiotics division." Pew Trusts reports that there are 42 new antibiotics in different phases of development, and only one of these is being produced by a large company with a sustainable supply chain.[8] Government entities need to provide incentives for larger companies to research and produce new antibiotics along with a strong supply chain to ensure a sustained production of essential antibiotics.

Decreasing the Use of Environmental Antibiotics

The environmental use of antibiotics refers to using antibiotics in livestock. In 2015, it was noted that 70% of total ingested antibiotics actually came from the consumption of animal products.[9] Over the next decade, it is estimated that consumption of antibiotics from livestock will increase by roughly 70%.[10,11] The FDA has made significant efforts in curbing the use of antibiotics in animals. For example, since 2017, it has been illegal to use "medically important" antibiotics for the growth of livestock. The FDA defines "medically important" antibiotics as those that are used frequently to treat human infections. Since the implementation of this law, there has been a 43% decrease in the sales relating to livestock containing antibiotics.[12] Another issue is the unnecessary use of antibiotics on livestock. Many farmers find it economically viable to prophylactically treat all their livestock rather than having to quarantine and treat once the infection becomes present.[13] Educating farmers on antibiotics might help curb this problem. Table 1 lists countries with the highest use of antibiotics in livestock and the drug resistant index. It is vital to identify ways to further reduce the amount of antibiotics used in livestock to prevent further progression of AR.

Proper Antibiotic Stewardship

There are several things that health professionals can do regarding proper antibiotic prescribing. They can be more discerning in how often they prescribe antibiotics, closely monitor for AR, keep a clean healthcare environment, talk with their patients regarding proper antibiotic use, and discuss ways to prevent infection including improving personal hygienic practices.

Recent studies have indicated that 30%–70% of prescribed antibiotics at the hospital are suboptimal: using broad-spectrum antibiotics for empiric therapy when a narrower spectrum antibiotic would be appropriate.[14-16] Consideration for earlier

Table 1: Antibiotic use in livestock and in hospitals globally

Countries	Livestock antibiotic use (mg/kg of livestock)[19]	Medical antibiotic usage (defined daily dosage/1000 people)[20]	Drug-resistant index[21]
Spain	182	14,634	48
Italy	157	11,191	47
France	41	13,040	42
Australia	13	11,088	35
The United States	88	10,298	13
Canada	119	7078	10
Sweden	8	4722	6

The drug-resistant index is a validated method of measuring the ability of antibiotics to effectively treat an infection that they are indicated for

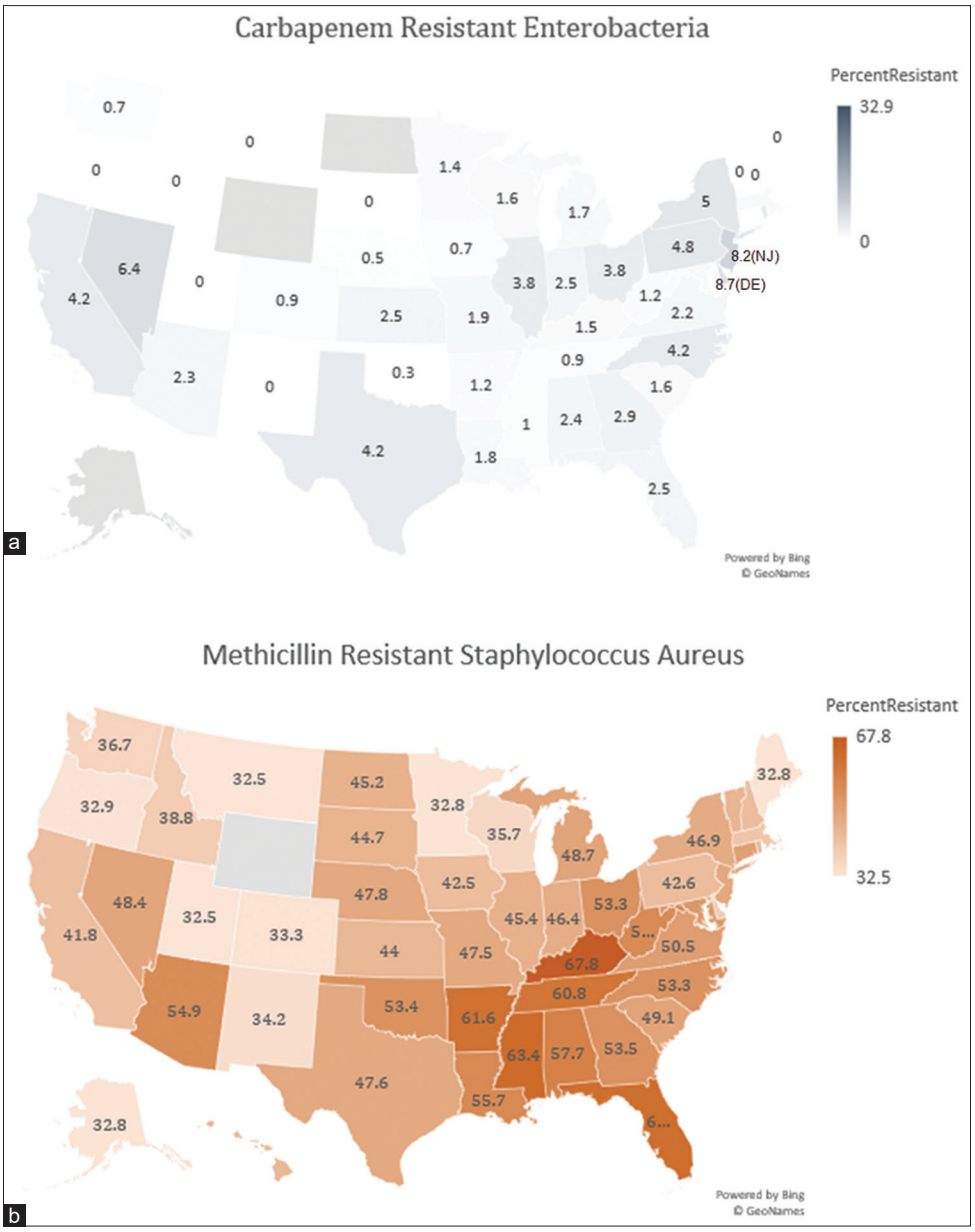

Figure 1: (a) This figure shows the percentage of resistance (2014) in each state when comparing all health care-associated infections. Nevada and the Northeast states seem to have the highest rates of resistance. (b) This figure shows the percentage of resistance (2014) in each state when comparing all health care-associated infections. Southern states seem to have the highest rates of resistance

infectious disease referral should be undertaken not only for complicated cases but also for uncomplicated infections when there is a question regarding the optimal antibiotic prescription.[14] Proper education regarding the surrounding hospital community being treated as good levels of AR should be reviewed with the medical staff.[15] The United Kingdom currently uses specialized pharmacists to train the health-care professionals in antibiotic choice, thus reducing health care-associated infections, particularly *Clostridium difficile* infection.[16]

Policy-makers can also do their part by creating methods to improve surveillance, prevent and control of outbreaks, promote regulation of cleanliness and hygiene in hospital settings, and distribute information to the public about AR. An example of a surveillance measure is the Centers for Disease Control and Prevention's AR maps which show AR [Figure 1].[17] Proper antibiotic stewardship is a combination of awareness of the individual prescriber, as well as education and research on a national and even global level. An example is legislation such as the Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms Act (DISARM) introduced in 2019 to promote AR research.

In conclusion, addressing these three problems of increasing incentives for research and production of antibiotics, decreasing environmental antibiotic usage, and proper antibiotic stewardship are vital to decreasing AR globally and

locally. We believe that with continued collaborative efforts, we will hopefully reduce the threat of AR in the coming years.[18]

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Conflicts of interest

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