Overuse and Misuse of Antibiotics, their Implications on the Development of Antibiotic Resistant Bacteria and the Current Antibiotic Stewardship Practices to Alleviate the Issue

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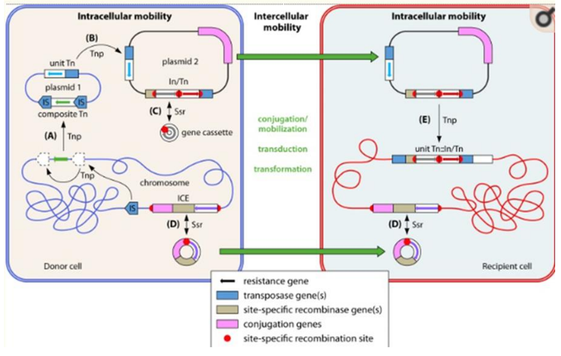
Multi-Drug Resistant Pathogens

Overuse and misuse of antibiotics leads to multi-drug resistant pathogens. Common factors that aid in the development of multi-drug resistant pathogens are prior use of antibiotics, lengthy hospital stays, and prior intensive care unit stays. The U.S. Centers for Disease Control and Prevention provided a list of the rising multi-drug resistant Gram-negative bacteria threats: *Enterobacteriaceae*, *Acinetobacter*, and *Pseudomonas* (Li et al. 2015). Multi-drug resistant pathogens cause a dual sided problem. On one hand, antibiotic use needs to be lessoned in order to decrease resistance, but on the other hand antibiotic resistant bacteria make it difficult to develop new treatment options.

Mobile Antibiotic Resistance Genes

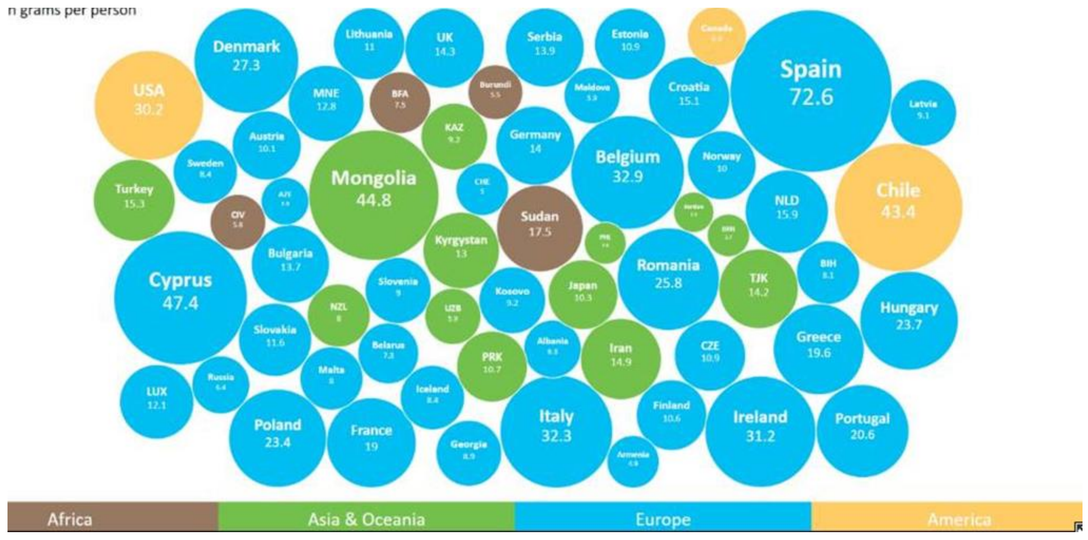
According to Partridge et al. (2018) the ability of Gram-positive and Gram-negative bacteria to change and acquire new properties and withstand treatments is achieved through the joint activities of mobile genetic elements. These elements work together and allow for the capture, accumulation and dissemination of resistance genes.



This figure shows examples of mobile genetic elements and how intercellular and intracellular mobility work (Partridge et al. 2020).

Introduction

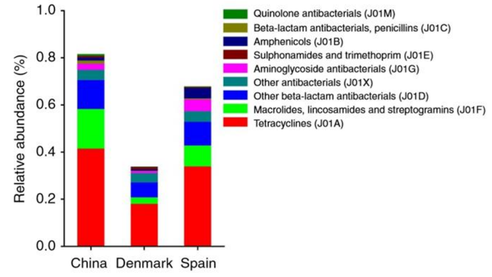
Misuse and overuse of antibiotics occurs worldwide and in a variety of ways. It has been reported as a cause of the emergence of antibiotic resistant bacteria. If actions are not taken to alleviate the rise of drug resistance, the number of deaths due to drug resistant infections is estimated to go from the current 700,000 to 10 million by 2050 (Goff et al. 2016).



This figure shows examples of antibiotic footprints measured in grams per person. The data is from 2015, based only on open access data for each country shown (Limmathurotsakul et al. 2019).

Changes in Gut Microbiota

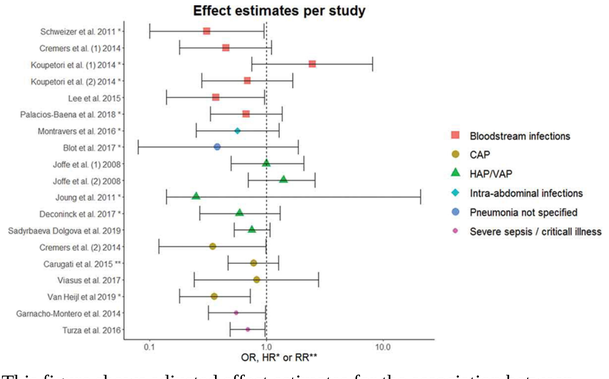
Scientists and researchers are paying closer attention to the gut microbiota as a reservoir for antibiotic resistance genes. Antibiotic resistance genes within the human gut bacteria can not only exchange within the microbiota inside the gut, but it can also be transferred to other bacteria that are passing through the intestines (Lu et al. 2014). Antibiotic resistance genes found in human gut microbiota change between different countries. This could be due to different selections and pressures of antibiotics (Hu et al. 2013).



This figure shows the relative abundance of resistance gene types assigned to certain types of antibiotics in the three countries (Hu et al. 2013).

Antimicrobial Stewardship

Antimicrobial stewardship programs have been implemented by US hospitals as Columbia University Medical Center, Wake Forest Baptist Medical Center and Johns Hopkins Hospital. One successful program is de escalation to improve antibiotic use in patients. Heijl et al. (2020) used observational data to study the associations between de escalation of empirical antimicrobial therapy and mortality. All variables need to be considered when making the decision for de escalation. These variables include confounds, which can be time fixed or time varying, culture results, and clinical stability. Directed acyclic graphs are used to depict the factors involved in the association between de escalation of empirical antimicrobial therapy and mortality.



This figure shows adjusted effect estimates for the association between de escalation of empirical antimicrobial therapy and mortality.

Conclusions and Recommendations

Infections that are caused by multi-drug and antibiotic resistant bacteria increases morbidity, mortality, and healthcare costs (Partridge et al. 2020). Overuse and misuse of antibiotics can be seen in many forms. Stewardship practices, if not implemented and taken seriously, will increase the severity of antimicrobial resistance. Heijl et al. (2020) recommends that clinicians and researchers should determine a standardized definition for de escalation and clinical stability for specific infections.

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