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Emerging frontiers of antibiotics use and their impacts on the human gut microbiome

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ABSTRACT

Antibiotics, the primary drugs used to cure bacterial diseases, are increasingly becoming ineffective due to the emergence of multiple drug resistance (MDR) leading to recurrence of previously sensitive pathogens. Human gut microbiome (GM), known to play an important role in various physiological processes, consists of pool of diverse microbes. Indiscriminate use of antibiotics during the life span of an individual may lead to development of resistant microbes e.g. *Vibrio, Acinetobacter, Escherichia, Klebsiella, Clostridia,* etc. in the human GM. Transmission of antibiotic resistant genes (ARGs) between pathogenic and commensal bacteria occurs more frequently in microbiome communities wherein bacteria communicate and exchange cellular constituents both among themselves and with the host. Additionally, co-factors like 'early vs. late' exposure, type of antibiotics and duration of treatment modulate the adverse effects of antibiotics on GM maturation. Furthermore, factors like mode of birth, ethnicity, malnutrition, demography, diet, lifestyle, etc., which influence GM composition, can also indirectly alter the host response to antibiotics. Currently, advanced 'omics' and culturomics approaches are revealing novel avenues to study the interplay between antibiotics and the microbiome and to identify resistant genes in these bacterial communities. Here, we discuss the recent developments that have given insights into the effects of antibiotics on the homeostatic balance of the gut microbiome and thus on human health.

1. Introduction

Antimicrobial compounds have been used to clear and cure numerous infectious diseases since antiquity. Following the discovery of the first antibiotics in 1928 (penicillins), they have become an integral part of the treatment regime for several diseases. The continuous consumption of antibacterials has since increased significantly and their arbitrary applications turned out to be critical disruptors of human gut microbiome homeostasis (Zarrinpar et al., 2018). While studying host gut bacteria today, it is vital to reconsider Koch's postulates, whereby the applications of a particular antibiotic were thought to eradicate specific pathogens. Although antibiotics primarily target particular pathogens, the growth and colonization of diverse and symbiotic bacterial congregations in the gut are also indiscriminately harmed. Additionally, it has been observed that the frequent usage of antibiotics cocktail along with other factors such as malnutrition, age, geneology and invasion of pathogens leads to lower resilience and decreased colonization resistance, which modulate bacterial ecology of gut (Vonaesch et al., 2018; Zhang et al., 2021). Notably, the effects of antibiotics on the microbiome depend on the type and combination of antibiotics, mode of administration and duration of treatment. Therefore, occupants of the new bacterial consortia and their 'evasion-and-invasion' lead to the addition of novel resistance genes to the preexisting dynamic and evolving resistomes and pathogenic bacterial phenotypes.

The gut microbiome is a highly complex and dynamic microbial community encompassing almost 39 trillion microbial cells, which includes bacteria, viruses, fungi that live in and on us. The co-existence of

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