A Versatile Population Dynamics Model of Bacterial Resistance, Tolerance, and Persistence

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In recent decades, there's been an alarming increase in bacterial evasion of antibiotic treatments, necessitating an improved understanding of resistance, tolerance, and persistence. Resistance confers an increase in the minimum inhibitory concentration (MIC), the minimal antibiotic concentration required to inhibit bacterial growth. On the other hand, persistence and tolerance both prolonged the minimum duration for killing (MDK), the duration of lethal antibiotic application required before bacterial death. While persistence is a phenotypic switch that confers temporary dramatic increases in MDK, tolerance develops through mutation and is more permanent. A growing body of research has shown that tolerance and persistence heavily influence the evolutionary trajectory of a bacterial population, facilitating both resistance development and long-term survival. To identify the specific effects of resistance, tolerance, and persistence on the characteristics of a bacterial population, a mechanistic and stochastic agent-based computational model was developed. The model indicated that persistence played a significant role in the survival of the bacterial population, while tolerance was more influential in the evolution of resistance. Additionally, a new metric, the dose-dependent MIC (ddMIC), was created, which incorporates the exponential decay of antibiotic concentration observed in the human body, making it more pertinent in clinical settings. In the model, the ddMIC was the optimal concentration for resistance development. These specific insights into bacterial population dynamics, which can easily be adapted to different bacterial strains and antibiotic treatments, will allow us to develop more individualized strategies to combat pathogenic bacterial infections.

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