Patient Non-Adherence to Multi-Drug Therapy and the Evolution of Multi-Drug Resistant Tuberculosis | Regina Joice

Despite the fact that drugs have been available to treat tuberculosis for over fifty years, the so called “White Plague” of the 17th century still manages to kill two million people every year. Many nations are unable to provide treatment to the growing proportion of their citizens with tuberculosis. Others are able to provide treatment but neglect to follow-up on patients to insure successful completion of the complicated drug regimen. Health department negligence of tuberculosis is partly blamed for the surge of tuberculosis rates in the U.S. in the 1980’s. However, patient negligence of tuberculosis in the form of non-adherence to drug regimens has become an increasingly worrisome problem.

Patient non-adherence to multi-drug therapy for tuberculosis has been shown to contribute to the evolution of multi-drug resistant strains in mathematical models of within-host population dynamics. However, the patterns of non-adherence that have been modeled in the past are not representative of actual patient dosing habits as observed in studies using electronic monitoring systems. Research has confirmed that treatment outcomes for non-adherent patients depend greatly on temporal dosing patterns.

Therefore, the purpose of this paper is to model common patterns of non-adherence and investigate which patterns result in higher rates of multi-drug resistant tuberculosis. The models presented in this paper illustrate the evolution of multi-drug resistance in three observed patterns of patient non-adherence: drug holidays, early termination, and white coat adherence, and one theoretical pattern: random non-adherence. Random non-adherence serves as a representation of adherence given as a percent, without any information on temporal dosing pattern.

White coat adherence and random non-adherence led to the evolution of multi-drug resistance more often than drug holidays. Early termination never resulted in multi-drug resistance. The patterns that contained long periods of continual perfect adherence resulted in the lowest rates of multi-drug resistance. Random non-adherence resulted in the highest rates of resistance, indicating that it may not be the best representation of a typical pattern of non-adherence.

Along with investigating the likelihood of various adherence patterns to result in the evolution of multi-drug resistance, I also explored the reasons for non-adherence and the possible strategies to improve adherence. After examining the costs and ethics of adherence improvement strategies, I recommend electronic monitoring systems for improving adherence and reducing rates of drug-resistance. The combined use of these systems and simulation software could allow patients and physicians to best work together to assess the patient’s risk of evolving resistance.