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New Paradigms in Simulating the Prediction, Intervention and Control of Infectious Diseases

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New Paradigms in Simulating the Prediction, Intervention, and Control of Infectious Diseases

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Abstract

Mathematical models based on the underlying transmission mechanisms of the disease can help the medical/scientific community understand and anticipate the spread of an epidemic and resistant strains in different populations and evaluate the potential effectiveness of different approaches for bringing an epidemic under control. Even more important than the successes with these specific diseases has been the development of frameworks and concepts for understanding epidemiology. Modeling can reduce the uncertainty of the estimates of disease prevalence and aid in the development of scientific understanding of the mechanisms of the disease and of the epidemic. It can also estimate the benefits and the costs of projected interventions and project the requirements that an epidemic will place on the health care system. Thus, the modeling techniques can join with biological, epidemiological, behavioral, and social science studies to produce better projections and better understanding of the epidemic. The new models and analysis in this research has lead to advances that will help us to better understand the spread of infectious diseases, including influenza, hepatitis, HIV and other sexually transmitted diseases, and to be able to estimate and subsequently predict the impact of control measures on their spread.

Background and Research Objectives

Infectious diseases continue to be an urgent public health problem. New diseases, such as Hantavirus and mad cow disease, spread by prions, are constantly being recognized. Known diseases, such as gonorrhea, tuberculosis, and bronchitis have developed resistance to the so-called miracle drugs that once held them in check. Influenza, HIV, and the common cold have proven difficult to immunize against and to treat once they occur. It has become important to use all of the tools available to devise effective strategies to minimize the impact and spread of infectious diseases, and to predict and understand the development and spread of resistant strains. Mathematical models based on the underlying transmission mechanisms of the disease can help the medical/scientific community understand and anticipate the spread of an epidemic and resistant strains in different populations and evaluate the potential effectiveness of different approaches for bringing an epidemic under control. Examples of diseases analyzed by epidemiological models include malaria, rubella, influenza, measles, hepatitis, and gonorrhea.

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Equally important to the successes with these specific diseases has been the development of new frameworks and concepts for understanding epidemiology. In this research we concentrated on the spread of HIV in a heterogeneous population and modeled the effectiveness of random screening and active contact tracing to slow the spread of the virus. We also confirmed that isolation strategies based on sequestering individuals infected with HIV would have minimal impact of the epidemic.

Importance to LANL's Science and Technology Base and National R&D Needs

A theoretically justified model will be a significant step in identifying the early detection, attribution and control of an epidemic initiated by terrorist attack or in biological warfare. Biological terrorism and proliferation is an emerging issue of national importance in which we can provide scientific leadership in mathematical modeling and in which we can make a significant impact. We addressed critical questions concerning the transmission (the ability of individuals to expose others to the infection), susceptibility (the biological and physical mechanisms that protect an individual from infection), progression (the rate at which the infection produces symptoms in individuals) and effectiveness of different interventions. Areas in which modeling will continue play a role in increasing our understanding and in providing feasible forecasts include:

- Optimizing the impact of prevention strategies on future disease transmission.
- Assessing the impact of proposed medical interventions.
- Optimizing epidemiological sampling strategies and investigating their cost effectiveness.
- Assisting in the understanding of the early history of an outbreak and identifying the initial infection.
- Estimating the degree to which the disease will spread among different populations.
- Predicting the dynamics of the epidemic by analyzing small-area geographic dispersion of infection.
- Investigating with statistical and modeling techniques biological phenomena, including the genetic variation within virus strains, or different systems of staging incubation periods.
- Assessing the impact of partial protection to infection by vaccination or protective clothing.

Scientific Approach and Accomplishments

Recent studies of HIV RNA in infected individuals show that viral levels vary widely between individuals and within the same individual over time. Individuals with higher viral loads during the chronic phase tend to develop AIDS more rapidly. If RNA levels are correlated with infectiousness, these variations explain puzzling results from HIV transmission studies and suggest that a small subset of infected people may be responsible for a disproportionate number of infections. We developed two simple models to study the impact of variations in infectiousness. In the differential infectivity (DI) model, we accounted for different levels of virus between individuals during the chronic phase of infection, and the increase in the average time from infection to AIDS that goes along with a decreased viral load. The staged progression (SP) model followed the more standard hypothesis that infected individuals progress through a series of infection stages, with the infectiousness of a person depending upon his current disease stage. We derived and compared threshold conditions for the two models and find explicit formulas of their endemic equilibria. We showed that formulas for both models can be put into a standard form, which allows for a clear interpretation. We compared the relative impact of each group as the fraction of infections being caused by that group. We use these comparisons and numerical simulations to examine the relative importance of different stages of infection and different chronic levels of virus to the spreading of the disease. The acute stage and the most infectious group both appear to have a disproportionate effect, especially on the early epidemic. Contact tracing to identify superspreaders and alertness to the symptoms of acute HIV infection may both be needed to contain this epidemic.

We analyzed the impact of various levels of intervention programs on the early epidemic and the endemic equilibrium. We also simulated numerically the time evolution of several scenarios, and examined the effectiveness of contact tracing in identifying the most infectious group transmitting the infection. These studies led us to the following conclusions:

- Random screening and contact tracing can be included in simple STD transmission models.

- Contact tracing is most effective when there are core groups of individuals remaining in for long periods of time that are transmitting the majority of the infections.

- Contact tracing is only slightly more effective than random screening when a large fraction of the infections are transmitted by individuals in a short, highly infectious early stage within the disease progression.

- When using models to guide intervention strategies, the model must capture the underlying etiology of the disease transmission before it can be used to estimate the impact of the intervention on the epidemic.

Thus, we have illustrated how mathematical models based on the transmission mechanisms of HIV can help the scientific community evaluate the potential effectiveness of different approaches for bringing an epidemic under control. It would be possible for public health officials or economists to add dollar amounts to various levels of screening and contact tracing in a particular population, and estimate the cost of reducing the epidemic to certain levels using these two models. However, we caution that the real epidemic is more complex that the models we have studied here, in part because of the complexities of sexual partner selection. Also, although we have separated the DI and SP mechanisms in order to understand each of their roles, it appears from the data that HIV infected people both go through stages and have different individual levels of virus during the chronic infection stage. We are currently developing and analyzing a combined DI and SP model. . The insights we have gained from these simple modes are just one step in improving our understanding of the essential relationships between the social and biological mechanisms that influence the spread of the disease and can help set priorities in research, saving time, resources, and lives.

Publications

" The Impact of Random Screening and Contact Tracing in Reducing the Spread of AIDS," with J. M. Hyman, J. Li and E. A. Stanley. Los Alamos Report LA-UR-99-5351 (1999), in review.

"Sensitivity Studies of the Differential Infectivity and Staged Progression Models for the Transmission of HIV," with J. M. Hyman, J. Li and E. A. Stanley. Los Alamos Report LA-UR-99-2253 (1999), in review.

"An Intuitive Formulation for the Reproductive Number for the Spread of Diseases in Heterogeneous Populations," J. M. Hyman and J. Li. To appear Math. Biosciences (1999).

"The Differentiatial Infectivity and Staged Progression Models for the Transmission of HIV," J. M. Hyman, J. Li and E. A. Stanley, Mathematical Biosciences **155**, no. 2 (1999) 77-109.

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