The community-wide dilemma of hospital-acquired drug resistance

Leslie A. Real*
Department of Biology, Center for Disease Ecology, Emory University, Atlanta, GA 30322

Few of us who even casually read the newspaper harbor the long-cherished belief that infectious diseases are a problem of the past. Infectious diseases, even during the most optimistic times, remained the major worldwide source of human mortality. At present ∼17–20 million people die annually of infectious diseases, mostly as a consequence of well recognized diseases: malaria, tuberculosis, and HIV. A recent report (1) highlights the continued and even escalating threat to human health from an expanding list of human pathogens. These threats are largely the consequence of the emergence of novel pathogens into the human population (e.g., SARS-CoV and HIV), the transport of pathogens into novel areas (e.g., West Nile Virus), or the evolution of resistance among pathogens once believed controllable (e.g., antimicrobial-resistant forms of tuberculosis). In the wake of this enormous problem, there has been a renewed effort at constructing mathematical models of the infectious disease process in an attempt to predict disease emergence and the evolution of antimicrobial resistance (2–12). Models of antimicrobial resistance have largely focused on the likelihood and conditions under which resistant pathogenic forms will arise and spread and the identification of measures that should be taken to limit emergence (9–11). Most often these models are targeted at individual patients, and the recommended controls are on the structure of drug delivery or they are targeted at specific subpopulations, for example, the aggregate of all patients in a particular hospital. Antimicrobial resistance in nosocomial diseases (i.e., infections that are acquired in hospitals) is a particularly alarming occurrence that appears to be increasing in frequency across a variety of pathogenic agents (Fig. 1) (13). In this issue of PNAS, Smith et al. (14) expand the modeling of antimicrobial resistance in nosocomial diseases to include the community context and economic costs of treatment across multiple hospitals rather than a single patient or hospital setting. Most policy recommendations for combating the spread of antimicrobial resistance (15, 16) target individual patients or highlight the importance of engaging individual hospital infection control (HIC) committees. The analysis by Smith et al. (14) suggests that such individualized hospital policy strategies are not very likely to succeed and will succumb to the tragedy of the commons (17–19), and that we must have a community-wide integration and coordination of policy.

If antibiotic-resistant bacteria are not highly transmissible, then the allocation toward hospital infection control can decrease.

Smith et al. (14) start with a simple phenomenological observation: Cities are plagued with much higher incidence of antimicrobial resistance than are rural areas. On a percentage basis, there are more carriers of antibiotic-resistant bacteria (ARB) in urban hospitals. Why is this? They acknowledge that there are epidemiological reasons for this widespread pattern, i.e., the greater number and density of hospitals and patients in urban areas may lead to a higher contact rate with carriers of ARB. However, in a very creative and insightful extension, they suggest that there may be economic, as well as epidemiological, explanations for this variation in the distribution of ARB.

Every hospital is faced with two conflicting objectives: first, to maximize the containment of ARB both in the hospital and the community, and, second, to minimize the costs of doing so. The strategy for meeting these two goals will be a complex decision involving the length of treatment of patients with ARB, the costs of treatment and control, the proportion of patients that acquire ARB, the transmissibility of ARB, and the strategies used by other hospitals in the region. There are some simple and obvious solutions to this decision problem. For example, if ARB is not highly transmissible, then spread is unlikely, and the allocation toward HIC can decrease. Alternatively, if the pro-
portion of patients that acquire ARB or the proportion of patients that are admitted asymptomatic but already colonized with ARB is very low, then the hospital need not allocate scarce resources into HIC. However, if the proportion of patients (drawn from the larger population in the community) that arrive at the hospital asymptomatic but already colonized with ARB is above a critical threshold, then the hospital is effectively swamped with ARB, and there is no point in trying to control it within the individual hospital. The existence of a threshold suggests that there are break-points in the system where the optimal solution for the individual hospital is to do nothing at all. The critical control variable then is the proportion of asymptomatic patients circulating among hospitals and in the common catchment population already colonized with ARB. This critical variable, however, is not the product of any individual hospital’s decisions, but is the consequence of the collective actions of all of the hospitals in the community. Herein lies the great dilemma.

When there are many hospitals in the community, as there are in urban areas, then each individual hospital has an incentive to reduce its HIC and let the other hospitals carry the economic burden of control. As a consequence of reduced HIC at the individual hospital level, more patients will be released into the common pool of patients that are now colonized with ARB; the more “cheating” in the system, the higher the equilibrium level of freely circulating ARB. Eventually, the critical threshold will be crossed, and the system will be swamped.

The conflict between the goals of the individual hospital versus the common goal of community-wide management of ARB is very much like a common property resource problem. When an individual hospital reduces its costs by reducing HIC, it does so by increasing the discharge of patients carrying ARB into the wider community. It is like pollution, where no individual polluter radically affects the system, but collectively the system is disastrously unhealthy. The pool of untreated patients released into the hospital commons can reach a threshold where ARB is uncontrollable even though every individual institution is acting optimally with regard to its own interests.

The implication of these conflicts that arise out of the multiinstitutional setting is the requirement for higher-level integration of information and control. The implementation of large-scale control measures involving multiple interacting but independent entities requires governance (18, 19). Indeed, the solution to the common property resource problem requires institutional regulation often in opposition to the interests of the individual parties. As Smith et al. (14) have illustrated, unless such interinstitutional governance is implemented, we can expect the increase in antimicrobial resistance to remain an escalating public health problem.