



Rising plague

The global threat from deadly bacteria and our dwindling arsenal to fight them

Brad Spellberg

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The problem of multi-drug-resistant bacteria, and the declining rate of antibacterial drug discovery, is an area of great concern to those caring for affected patients. The Institute of Medicine and the Infectious Diseases Society of America (IDSA) consider antimicrobial resistance a threat to US public health and security. In Brad Spellberg's *Rising plague*, both this problem and potential solutions are presented clearly. Spellberg, an associate professor of medicine in the divisions of general internal medicine and infectious diseases at Harbor-UCLA Medical Center and Los Angeles Biomedical Research Institute, is an academic physician-scientist who also sees patients. He is the coauthor of the *Boards and wards* series of medical review books and has been featured in "Rise of the Superbugs" on NOVA.

Rising plague outlines the problem of multi-drug-resistant bacteria by reviewing statistics and epidemiology and by relating poignant and dramatic stories of patients with antibiotic-resistant infections that the author himself has seen. The increasing prevalence of antibiotic-resistant bacteria, and the stalled production of new antimicrobial agents to treat these pathogens, is presented in a conversational style that is easily understood by the layperson. The purpose is to increase awareness and appeal to the general public to effect action and legislation to confront this important dilemma. For these reasons, it is also of interest to the scientific community.

The book begins with compelling patient stories: a young woman who died of a health care-associated infection by multi-drug-resistant *Acinetobacter baumannii*, and a previously healthy mother with a prolonged and disabling community-acquired infection by methicillin-resistant *Staphylococcus aureus*. The stories set the stage for a

review of the current prevalence of infectious diseases and an interesting overview of the history of antimicrobial therapy. The IDSA's "Bad Bugs, No Drugs" campaign is reviewed, as is its Web page concerning the Strategies to Address Antibiotic Resistance Act (STAAR Act; <http://www.idsociety.org/STAARAct.htm>), as Spellberg relates more stories of patients severely affected by multi-drug-resistant bacterial infections.

Factors leading to declining antibacterial drug development are examined in detail, including the perspectives of industry, IDSA, academic infectious disease specialists, and the NIH. There has been a 67% reduction in new antibiotics in the United States between 1983 and 2002, and the trend is worsening. IDSA and other medical professional groups support the STAAR Act, which would create and coordinate federal resources to fight antibiotic resistance.

Spellberg addresses the multiple reasons why research and development on antibacterial agents have declined in the pharmaceutical industry, including the scientific challenge in identifying new molecular candidates, inadequate funding in basic and translational research in bacterial antibiotic resistance, and the absence of a federally funded network of investigators for clinical trials of new antibiotics (as exists for HIV therapies). Antibiotics have the additional drawback of a lower return on investment due to short courses of curative therapy compared with the long-term, noncurative therapies given for chronic diseases such as hypertension and AIDS.

So, what are the proposed solutions? A federal commission of experts could delineate a list of priority multi-drug-resistant pathogens and priority antibiotic development that would be eligible for government incentives to the pharmaceutical industry,

from the point of drug discovery through to FDA approval. The Orphan Drug Act could be expanded to include priority antibiotics, and these antibiotics could be made a priority by the Biomedical Advanced Research and Development Authority (BARDA). To address rare but serious side effects not detected during premarketing clinical trials, a communal insurance policy could be established for antibiotic injury that occurs after marketing, analogous to the Vaccine Injury Compensation Program. Transferable patent extensions — allowing pharmaceutical companies to transfer a patent extension to a drug of their choice — would be a powerful incentive, but is controversial.

The book is successful at relating the problem of antibiotic resistance in a way that is easily accessible to the general public. The patient stories are compelling, and the information provided to describe the problem is thorough and referenced. The factors contributing to the difficulty with antibiotic drug development are described, and the potential solutions proposed are thoughtful and reasoned. Although issues are represented fairly, it would be helpful for the reader to know of the author's disclosures at the outset, rather than being presented with them more than halfway through the book. This is relevant because the proposed solutions involve incentives for industry.

Rising plague is an informed, thoughtful, and accessible review of the problem of multi-drug-resistant bacterial infection that affects patients in the hospital and the community, patients that are immunocompromised, and patients that were previously healthy. This book should prove a useful resource in mobilizing individuals to tell their own stories and to ask their legislators to take action that will finally provide resources to address this critical dilemma.