Microbes fight back

Revenge of the Microbes: How Bacterial Resistance Is Undermining the Antibiotic Miracle

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During the 1950s and 1960s, there was widespread optimism that antimicrobial agents would conquer infectious diseases. The 1970s and the 1980s saw the introduction of new classes of antimicrobials and new agents within each class. But optimism was soon tempered by the emergence and dissemination of multiresistant strains of bacteria.

Although antimicrobial drug resistance initially had its greatest impact in hospitals with the appearance of methicillin-resistant staphylococci (MRSA), vancomycin-resistant enterococci and multidrug-resistant Gram-negative organisms, it soon emerged in the community. By the 1980s, a high degree of resistance to penicillin in *Streptococcus pneumoniae*—the most common bacterial cause of lower respiratory tract infections in adults and otitis media in children—emerged. Shortly thereafter, worrisome multi-drug-resistant strains began to appear, and by the 1990s, penicillin resistance reached prevalence rates of more than 40% in many countries. MRSA infections have now disseminated amongst patients in hospitals worldwide, with prevalence rates greater than 80% in some healthcare facilities and reports of community-associated MRSA infections exceeding 50% in some regions of the United States.

Revenge of the Microbes: How Bacterial Resistance Is Undermining the Antibiotic Miracle takes us on a short journey from the excitement of the discovery of the first antibiotics in the 1930s to the crisis we face today with emerging resistance and a pharmaceutical industry reluctant to invest in this field. This compelling narrative is presented by two experts with extensive experience in antimicrobial resistance and education.

The authors first introduce their readers to the world of antibiotics; they describe what antibiotics are, the impact they have had on infectious disease scourges such as syphilis and tuberculosis, and their value today for the treatment of newly discovered infectious diseases such as gastric ulcers. They provide a fascinating account of the early days of research, from the unsuccessful attempts to discover antimicrobial agents in soil to the accidental discovery of penicillin in the laboratory and the subsequent years it took to realize the full potential of this new drug. They convincingly argue that it was inevitable that resistance to antibiotics would emerge, because of their bacterial and fungal origins, the billions of years they

have been around and over which microbes have had the opportunity to evolve resistance mechanisms and the recent widespread use and misuse in humans and in agriculture.

Although expressly written to provide an overview of the topic of antimicrobial resistance for a diverse audience including the lay public, the authors devote over half of the book to a detailed review of the major classes of antibacterials, in addition to antiseptics, antivirals, antifungals and antiprotozoal compounds. The antibacterials are described in a level of detail more appropriate for a biomedical readership, but the remaining antimicrobials receive only a cursory overview, with some topics, such as anti-HIV and antifungals, having less than a page allocated to them.

Antimicrobial resistance mechanisms are complex and in some cases have taken thousands of years to evolve. Microbes have also devised ways of sharing their multitude of resistance traits. This is an area of particular interest for the authors, and as such, it is dealt with extensively and comprehensively; the authors even digress to comment on the absurdities of the concern over resistance traits found in genetically modified foods and the insignificance of gene transfer should this ever occur—our own gastrointestinal tracts are already awash with microorganisms harboring a multitude of mobile antibiotic resistance mechanisms.

Finally, the authors address the reasons why many companies have abandoned antimicrobial drug discovery and development: the flat market forecast for antimicrobials; the skyrocketing cost for development of a new agent from bench to bedside; and stricter criteria from the US Food and Drug Administration for assessing safety and efficacy. But this must be a more complex issue than the authors suggest. The global antibiotic market is expected to grow annually by a rate of 9.1% to reach \$34.5 billion by 2006, a considerable incentive for companies to continue to invest in antibiotic drug discovery. Is it just a matter of being risk adverse or is it a failure to find new products to bring to market? Despite the initial enthusiasm for the application of structural and functional genomics to aid in the discovery of new agents, this avenue of research has yet to bear fruit.

Salyers and Whitt deliver a wealth of information regarding antimicrobial agents and mechanisms of resistance; however, I feel they would have come closer to their stated goal of “providing the scientific information readers will need to form opinions and make informed decisions regarding the use of antibiotics” if they had devoted more space to the causes and some of the solutions of the problem of antibiotic resistance. A number of important questions are not answered. For example, how has the misuse of antimicrobials led to this problem? What constitutes overuse? Have we, in some circumstances, used inappropriately low doses of antibiotics or the wrong bug-drug combination which has led to the selection and expansion of resistant subpopulations? Have we failed to adopt basic public health and infection control measures to minimize the dissemination of resistant strains? And which strategies to prevent or control the dissemination of resistance have worked in the past and which have not? An assessment of the magnitude of the problem with regards to the clinical and public health consequences would also have been of value. An abundance of surveillance and epidemiological data is available that would have provided more insight into this issue. The book will be of certain value to readers interested in learning more about drugs they have probably used at one time or another; however, a more comprehensive understanding of many of the issues the authors have touched upon will require further supplemental reading.

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