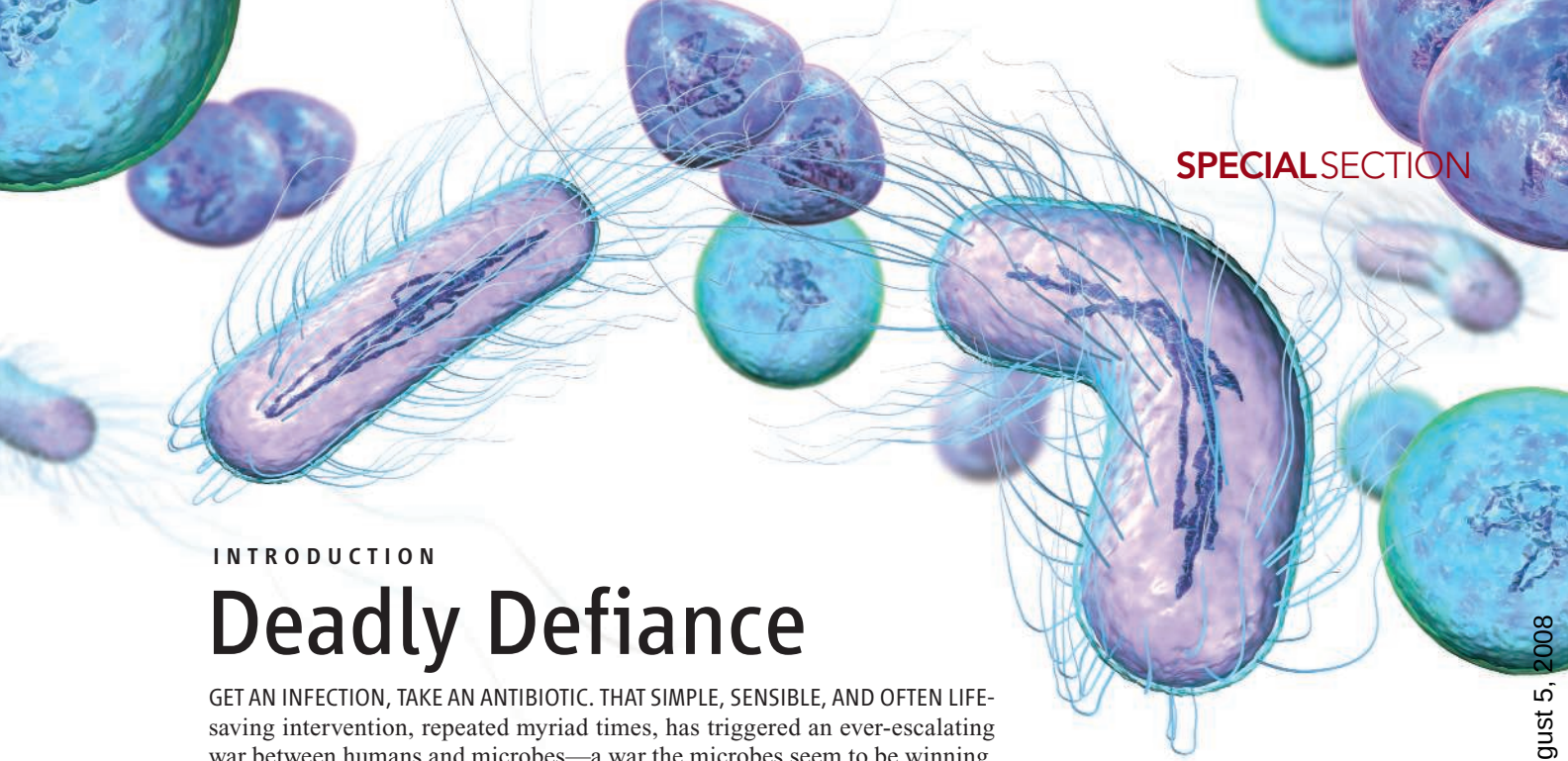

INTRODUCTION

Deadly Defiance

GET AN INFECTION, TAKE AN ANTIBIOTIC. THAT SIMPLE, SENSIBLE, AND OFTEN LIFE-saving intervention, repeated myriad times, has triggered an ever-escalating war between humans and microbes—a war the microbes seem to be winning. Almost as soon as penicillin was introduced in 1942, the bacteria it was designed to defeat began evolving to resist it. Now many common bacteria have acquired resistance to multiple antibiotics, making some infections extraordinarily difficult, if not impossible, to treat.

So far, most of these pernicious drug-resistant infections have been confined to hospitals, where opportunities abound for resistant bacteria to spread and enter the bloodstream or infect open wounds. But the recent emergence of multiple-antibiotic–resistant bacteria in the broader community, particularly methicillin-resistant *Staphylococcus aureus* in the late 1990s, has sparked considerable alarm, not to mention doomsday scenarios of untreatable bacterial infections arising from everyday scrapes and scratches.

In a News story in this special issue, Taubes chronicles the predictable, if unnerving, rise and spread of so-called bad bugs. As the number of antibiotic-resistant bacteria has increased, drug companies have been fleeing the field, leaving a dearth of new antibiotics, especially for the hard-to-kill Gram-negative bacteria. Short of a new wonder drug, the only near-term fix is to curb antibiotic use. Taubes describes several strategies, such as encouraging a switch from broad- to narrow-spectrum antibiotics and investigating the benefits of a shorter course of antibiotics instead of the standard 7 to 10 days.

In a second News story, Marshall goes behind the scenes with Partners in Health (PIH), a nonprofit organization associated with Harvard University's Brigham and Women's Hospital, in Tomsk, Siberia, visiting prisons, hospitals, and other hotbeds of multidrug-resistant tuberculosis (TB). Collaborating with local authorities, PIH has launched an innovative program for tackling this growing threat in places such as Siberia, where resources are limited. This includes roving community workers or nurses who track down recalcitrant patients and give them their medicine, as well as trying to optimize the use of existing (and outdated) drugs. PIH's persistence and vigilance have paid off, but it's unclear whether such a labor-intensive model can work elsewhere. Meanwhile, even in Tomsk, the percentage of TB cases that are drug-resistant remains high—not an auspicious sign.

Two Perspectives explore how resistance emerges and whether such mechanisms reveal possible new interventions. On p. 365, Martínez discusses the evolution of antibiotic resistance genes in bacteria in natural environments and considers whether this might offer clues for fighting infections in more familiar clinical settings. Monk and Goffeau (p. 367) look at modes of fungal drug resistance and whether broad-spectrum fungicides, yet to be developed, might be a solution.

–LESLIE ROBERTS AND STEPHEN SIMPSON

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Drug Resistance

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