Novel approaches needed to end growing scourge of 'superbugs'

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With the rising awareness of the so-called "superbugs," bacteria that are resistant to most known antibiotics, three infectious disease experts writing in the Jan. 24 edition of the *New England Journal of Medicine* called for novel approaches based on a "reconceptualization of the nature of resistance, disease and prevention."

"Antibiotic-resistant microbes infect more than 2 million Americans every year and kill more than 100,000 annually," said Brad Spellberg, M.D., a Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center lead researcher and one of the authors of the viewpoint article published in the New England Journal of Medicine. "They spread rapidly, even in such seemingly harmless places as high school locker rooms, where they infect young athletes, and they can make mundane urinary or intestinal infections life-threatening. At the same time, the development of new antibiotics to treat these infections is plummeting, leading to our call for entirely new approaches to the problem."

Dr. Spellberg, author of the book, "Rising Plague: The Global Threat from Deadly Bacteria and Our Dwindling Arsenal to Fight Them," authored the article with Drs. John G. Bartlett and David N. Gilbert, both past presidents of the Infectious Diseases Society of America.

The article's authors called for continuing the traditional practices in "infection control, antibiotic stewardship, and new antibiotic development." But they also write that the World Economic Forum's recent conclusion that antibiotic-resistant bacteria represent "arguably

the greatest risk…to human health" underscores the need for new approaches as well.

New interventions are needed "to prevent infections from occurring in the first place, to encourage new economic models that spur investment in anti-infective treatments, to slow the spread of resistance in order to prolong the useful lives of antibiotics, to discover new ways to directly attack microbes in a manner that does not drive resistance, or to alter host–microbe interactions in order to modify disease without directly attacking microbes," the researchers wrote.

Among their recommendations are stricter monitoring and controls for prescribing antibiotics and changes in hospital practices, including greater disinfection and less usage of invasive materials than can transmit antibiotic-resistant bacteria into the body.

They recommended new regulatory approaches to encourage antibiotic development, such as the Limited Population Antibiotic Drug (LPAD) proposal from the Infectious Diseases Society of America. They said this proposal would encourage the development new antibiotics by allowing their approval based on smaller, less expensive clinical trials.

They also called for new approaches to treating infections caused by bacteria. Rather than attacking the microbes causing the infection, the researchers urged scientists to pursue new courses of discovery that either "moderate the inflammatory response to infection or that limit microbial growth by blocking access to host resources without attempting to kill microbes."

"The converging crises of increasing resistance and collapse of antibiotic research and development are the predictable results of policies and processes we have used to deal with infections for 75 years," the authors write. "If we want a long-term solution, the answer is not incremental

tweaking of these policies and processes. Novel approaches, based on a reconceptualization of the nature of resistance, disease, and prevention, are needed."

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