



Opinion
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A Grateful Seasonal Plea to Friends in the Research Trenches

David Reynoso*

Department of Internal Medicine, University of Texas Medical Branch, USA

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*Corresponding author: David Reynoso, M D, PhD, Infectious Disease Division, Department of Internal Medicine, University of Texas Medical Branch, 301 University Boulevard, Galveston, TX 77555-0435, USA, Email: dareynos@utmb.edu

Opinion

In a season that evokes love, giddy joy, empathy, tolerance, and heartfelt conversations, a profound sense of gratitude for antibiotics engulfs me. From my day to day routine of clinical infectious diseases, to enjoying hammock time with my daughter, it is evident to me that our lives and future prosperity depend on antibiotics and on those in the research trenches working to overcome resistance through their defiant pursuits. I wish to thank those researchers here.

Prokaryotes, these basic single-celled organisms with no nucleus or cognitive volition, were thriving on Earth billions of years before us. We, the glorious eukaryotes, inherited and optimized their macromolecules, evolved sex from their cold modes of replication and division, usurped them as organelles into our cells, and adapted their electron transport chains for our energy production. We further formed multicellular platforms of organ systems, turned quorum sensing into language, formed communities that transformed and divided our planet (their planet), and began to explore other worlds.

To accomplish all of this through millennia, we had to work with prokaryotes. We carried them, and still do, in our intestines and on our skin.

The microbiome, we now know, protects us from serious pathogens and from our own immune system, and provides us with essential nutrients and co-factors, in a symbiotic equilibrium forged of shared experiences. Throughout evolution, without knowing the microbes were there, we knew we had to avoid piercing our integument to avoid infection. We knew, or probably learned, that a batch of fermented juice could beget another, or that dried or cooked meats were safer than putrid ones. I cannot help but ponder how broad the shoulders are of the

giants we stand on. Roughly 300 years ago, the microscope was as new fangled as Newton's *Principia*. I chuckle at the thought of Leeuwenhoek making clear observations on a world few imagined existed before; and I chuckle even more at the thought of him embellishing the observations to the astonishment of his nephews and nieces by the fireplace.

One-hundred years ago, there were no antibiotics, and people died frequently of complications of infections that are today considered mundane, such as pneumonias, appendicitis, and puerperal infections. The discovery of penicillin in 1928 is truly among the greatest gifts that humankind has ever received. But with its availability, and without much hesitation, we turned our backs on prokaryotes. We assaulted them with antibiotics, heavily and often for the past 88 years, first for venereal disease and then for everything else. We now use antibiotics even for conditions we know to be largely caused by viruses, such as colds or diarrhea.

Our greediness for unnecessarily-aseptic lives is perhaps the Grinch of this story, as it has led to a collective overuse and dependence on antibiotics, and facilitated the adaptive selection of microbes for which there are no existing therapeutic options. In other words, for some infections, we have regressed by a century. By some estimates, antibiotic resistance in the setting of ordinary infections will be the leading cause of death by midcentury. Alas, those battles will be fought in coming decades and need not ruin this particular season. I simply wanted to express my profound gratitude for antibiotics and for the researchers who have advanced, and are advancing, their development. This season, I am reinvigorated by the thought that, perhaps, the greatest gift we could receive is a challenge to secure the availability of antibiotics for the future.

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