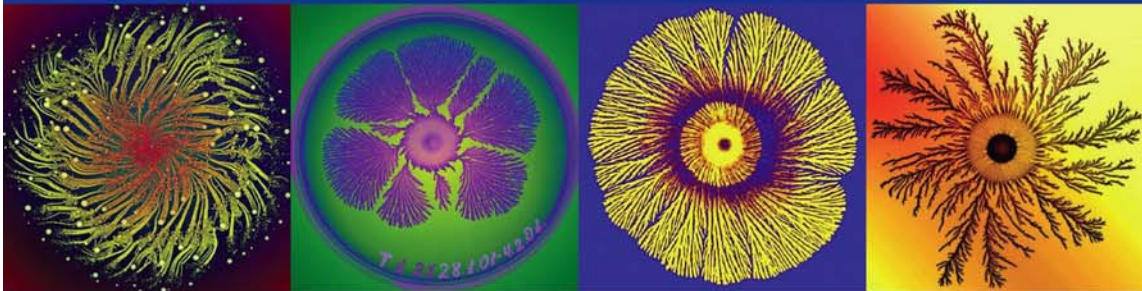


THIRD EDITION

# Beyond Antibiotics



Strategies for Living in a World  
of Emerging Infections  
and Antibiotic-Resistant Bacteria

**Michael A. Schmidt, PhD**

Author of *Brain-Building Nutrition*

# **Beyond Antibiotics:**

## **Strategies for Living in a World of Emerging Infections and Antibiotic Resistant Bacteria**

**Michael A. Schmidt, Ph.D.**

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## Introduction

The War on Germs cannot be won. And each of us is now affected.

Remarkably, we did not see this as a war that could not be won. Now, at a time when emerging infections and antibiotic-resistant bacteria are rising sharply, our development of new antibiotic drugs is nearly drying up. A recent study of the largest drug companies in the world revealed that only 6 of 506 new drugs in development were antibiotics. This is extraordinary. As infections are becoming more threatening, the supply of new drugs to treat them has fallen to a trickle.

Where does this leave those of us who want to protect ourselves and our families?

What can each of us do to curtail our use of antibiotics, so this problem does not accelerate?

What new set of tools must each of us have so that we can live safely in the **bacteria's world**?

And what if prior antibiotic use has led to poor health? Is there a straightforward path to recovery?

Before we answer these questions, we must understand why we have lost the war on germs and why we cannot win. We are living in a world where the bacterial “enemy” comprises some 90 percent of all living matter on earth. We are living in *their* world. We also failed to consider that our bodies are cloaked in a blanket of bacteria so pervasive that the bacterial cells outnumber our “human” cells by a factor of ten. The sheer numbers of bacteria are so vast that “victory,” however we might define it, is impossible.

The war on germs most certainly grew from noble roots. It expanded from treating the very sick, to treating the not-so-sick, to treating those who might get sick. Their use spread to animals, then to fruit trees, then to the fish we eat. As we learned about growing microbial threats, we took the war on germs into everyday life—dish soap, shampoo, toothpaste, and deodorant. Through all this, we did not know that we were training the “enemy.”

Suddenly, though not without warning, we were awash in a sea of microbes with an astonishing ability to resist our most potent drugs and to pass that capability for resistance to neighboring bugs. The casualties of our undeclared war on germs have clearly emerged. *We* are now the casualties of the war on germs. We have reached a point where some of us will become seriously ill or die because of antibiotic-resistant bacteria.

We don’t expect that it will be one of us, but we cannot predict whether we will be in an accident, sustain a cut, develop pneumonia, have a knee replaced, be weakened by diabetes, mourn the loss of a loved one, or encounter antibiotic-resistant bacteria that threaten our own lives.

Microbes, for all their tiny simplicity, behave as complex, adapting, and cooperative creatures, not unlike bees or ants. They are much more adaptable than we give them credit for and they are surely more adaptable than we are. When we use antibiotics unwisely, we are merely training this endless universe of bacteria to get better at what they do. Much as a musician or an athlete goes through endless hours of training to hone his craft, antibiotics provide the training ground for microbes in our midst to accelerate their training in how to best handle . . . **antibiotics**. If we want to train the next Beethoven of the bacterial world, we will surely do so unless we curtail our approach to antibiotic use—which is why the war on germs must end.

We must move *beyond antibiotics*, because nature has forced us to do so. Our tools have begun to fail and the bacteria have shown they will win. This has brought us to the **Post-Antibiotic Era**, in which untreatable infections are now commonplace. But what lies in this new world *beyond antibiotics*? To thrive in this new world, I propose we

now describe it as the **Era of Host Defenses**—where our first thought is of the host, the complex defenses of each one of us. We must marshal the vast body of research in the fields of nutrition, biochemistry, immunology, genetics, toxicology, psychology, exercise physiology, and related fields that permit us to propose a strategy of **personalized medicine** that can be used to build and balance the system of immune defense, energy, and repair.

We have surely entered an era of expanding scientific knowledge. With these great advances, however, we have still not solved the riddle of how we ultimately may defeat the microbes in our midst. It may be strongly argued that we will never do so. *Beyond Antibiotics*, then, is the emerging story of how we are to live *with them*. It is the story of how we will raise our defenses and coexist with the microbial world, while preserving the drugs of last resort that we so cherish.

*Beyond Antibiotics* is a roadmap, a way forward, and an important step in showing us how this can be accomplished.

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# Excerpt: Chapter 1

## Why the War on Germs Cannot be Won

We have declared war on an unbeatable foe—the microbe. It is now clear that this war cannot be won.

But there is a way forward.

Over a quarter century ago, the U.S. Surgeon General made a stunning announcement before congress that it was “time to close the book on infectious diseases.”<sup>i</sup> This heralded a kind of V-day (or perhaps B-day, for bacteria). It was a day long awaited, when we might declare victory against bacterial foes that had so devastated previous generations.

But a small chorus of stubborn dissenters would not join the celebration. Time quickly showed that our declaration was premature. A flurry of studies harkened the advance of emergent infections, more virulent microbes, and bugs that could thwart even our most potent antibiotic drugs.

In 1992, Dr. Harold Neu at Columbia University wrote a paper in the journal *Science* entitled “The Crisis in Antibiotic Resistance.” In this article, he pointed out that in 1941, only forty thousand units of penicillin per day for four days were required to *cure* pneumococcal pneumonia. “Today,” said Neu,

a patient could receive 24 million units of penicillin a day and die of pneumococcal meningitis.” He added that bacteria that cause infection of the respiratory tract, skin, bladder, bowel and blood “. . . are now resistant to virtually all of the older antibiotics. The extensive use of antibiotics in the community and hospitals has fueled this crisis.”<sup>ii</sup>

Doctor Neu was not alone. Also in 1992, Dr. Mitchell Cohen, a researcher with the National Center for Infectious Diseases at the Centers for Disease Control, issued this warning about antibiotics: “Unless currently effective antimicrobial agents can be successfully preserved and the transmission of drug-resistant organisms curtailed, the

post-antimicrobial era may be rapidly approaching in which infectious disease wards housing untreatable conditions will again be seen.”<sup>iii</sup>

A mere twenty-five years after the triumphal announcement of the Surgeon General came an urgent warning in the *Annals of Internal Medicine* with the sobering title, “The Conquest of Infectious Disease: Who Are We Kidding.”<sup>iv</sup> This was just the beginning of our recognition that the war on germs had, in fact, not been won and, perhaps, *could not be won*. Indeed, the sitting U.S. Surgeon General on the eve of 21<sup>st</sup> century declared that “We are seeing a global resurgence of infectious disease,”<sup>v</sup> while Nobel laureate Joshua Lederberg, PhD of Rockefeller University offered this scathing view of the present crisis in antibiotic-resistant bacteria: “We are on the road to an impending public health disaster.” Placing antibiotic-resistant infections in context with the dreaded Ebola virus, Dr. Lederberg vividly stated: “The odds of Ebola breaking out are quite low, but the stakes are very high. With antibiotic resistance, the odds are certain and the stakes are just as high.”<sup>vi</sup>

Authors of a report by the Institute of Medicine stated, “Pathogenic microbes can be resilient, dangerous foes. Although it is impossible to predict their individual emergence in time and place, we can be confident that new microbial diseases will emerge”<sup>vii</sup> Harvard professor and Nobel Laureate Dr. Walter Gilbert offered his dire assessment, warning that, “There may be a time down the road when 80 percent to 90 percent of infections will be resistant to all known antibiotics.”<sup>viii</sup> A chilling notion.

## **Infections Still Dominate Our World**

In this modern day of sophisticated medicine, it is almost unthinkable that infection by microbes still dominates our world. It is a testament to the fantastic vigor of microbes to adapt to seemingly impossible conditions.

Consider that:

- Infection is still the number one killer worldwide
- 50 percent of the United States health budget is spent on bacterial infections

- Hospital infections are now the fourth leading cause of death in the United States
- Collectively, infection is the third leading cause of death annually in the United States
- Food-borne microbial infections are responsible for an estimated **76 million** illnesses in the United States each year<sup>ix</sup>
- Infections are responsible for 30 percent of the deaths in senior citizens<sup>x</sup>
- Infections are the most common cause of hospitalization in older adults<sup>xi</sup>
- Infections in children are the most common reasons for visits to the doctor
- In the U.S., the estimated cost to employers of people with respiratory infections is over \$112 billion, including costs of medical treatment and time lost from work<sup>xii</sup>

## **The Startling Rise of Antibiotic-Resistant Bacteria**

MORE DEATHS FROM MRSA THAN FROM AIDS.

This was the headline that dominated the news in late 2007. An article in the *Journal of the American Medical Association* revealed that deaths from antibiotic-resistant staph aureus now account for more deaths in the U.S. than AIDS. This is extraordinary. Of some 100,000 cases of MRSA in the U.S. each year, there are over 18,000 deaths—more deaths than are due to AIDS. Consider also that:

- According to the World Health Organization, infectious diseases like malaria, tuberculosis, and pneumonia could have “no effective therapies within the next ten years.”
- Of the estimated 1.6 million nursing home residents in the U.S., 250,000 have infections, and 27,000 of them have antibiotic-resistant infections<sup>xiii</sup>

- In 1974, just 2 percent of the most common form of staph infections found in hospitals were resistant to the common antibiotic methicillin. Today, more than 60 percent are resistant to this drug
- Today, 70 percent of hospital infections are now resistant to at least one antibiotic
- For virtually every bug/drug combination resistance has been increasing over the last 4 or 5 years.
- A strain of ear-infecting bacteria known as strain 19A has now been found that can only be killed by an antibiotic (levofloxacin, Levaquin) approved for adults. This antibiotic has a warning on its label against use in children
- The United States alone spends **\$5 billion** annually to treat resistant bacteria.
- The cost of treating a patient with non-drug-resistant tuberculosis, about \$12,000, rises to \$180,000 for a patient with a multidrug-resistant strain of tuberculosis
- Since 2003, three U.S. National Football League (NFL) teams have reported multiple infections of MRSA
- 1 out of every 136 hospital patients becomes seriously ill as a result of acquiring an infection in the hospital. This is equivalent to 2 million cases and about 80,000 deaths a year.<sup>xiv</sup>

## **Bacteria are More Intelligent Than we Realize**

Bacteria are masters at adaptation and cooperation. When exposed to antibiotics that wipe out 90 percent of their population, the remaining 10 percent further adapt and form new colonies that can live in the presence of the antibiotic. In some cases, microbes can even subsist on chemicals we consider harmful to them.

Microbes are also genius at cooperation. They communicate with one another through many different “languages,” which includes an array of molecular signals. For instance, through quorum sensing, they can tell when population numbers are getting too large and slow their reproductive rate accordingly. Microbes are well known to produce

biofilms, where they layer themselves into protective niches so that harmful agents cannot penetrate and reach the central core.

One strain of microbe will even cooperate with another (as in the case of plaque in the mouth), forming biofilms that allow an entire colony of collaborating microbes of different species to thrive together. In this case, different species perform different tasks in support of the collective effort. New estimates suggest that as many as 20 different bacterial species collaborate to form the biofilm in dental plaque.

In the case of middle ear infection, for instance, bacteria seem to build cooperative biofilms that help them ward off threats in the middle ear, which may be one reason why antibiotics are ineffective in many earaches.

The microbes in a biofilm literally build castles as defenses out of specific molecules they manufacture from the raw materials in the host—the human. The bacteria use sugars (much like we would use bricks) and assemble them into multisugar branching chains to build up walls and towers (as we would assemble bricks into protective walls and towers). Bacteria seem to even organize scaffolding to raise the height of their towers—a remarkable feat. The cooperating bacteria in a biofilm encase themselves in a self-made fortress that keeps our bacteria-munching white cells and our chemical agents from permeating the barrier.<sup>§</sup> As for antibiotics, bacteria on the edges may be sensitive to our antibiotics, but those on the interior may be protected. The biofilms become all but impervious to antibiotics.<sup>xv</sup>

Beyond their cooperation building castles and towers, bacteria are masters at swapping genes with one another. They quickly adapt to harsh conditions by receiving genes from other microbes that might possess the ability to adapt to a given condition. Moreover, when conditions become too harsh, certain microbes form spores that are small, bowling-ball-like, impenetrable one-microbe islands. In this state, microbes can go without food or water for vast stretches of time. One reason antibiotics trigger severe intestinal bleeding in some people is that *Clostridium difficile* (an excellent spore former) lies dormant in the gut, in its impervious, docile, sporulated state. When an antibiotic

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<sup>§</sup> We will see later why strong host (human) defenses are important to establish as preventive measures, to ensure that bacterial invaders do not gain a foothold and that defenses mount before a biofilm can be formed.

wipes out the competing helpful bacteria in the gut, the *Clostridium* emerges from its spore state with little competition, begins munching on abundant nutrients, and produces toxic proteins that ravage the gut lining. The bowling ball becomes a Tasmanian devil.

Microbes can also send out all sorts of signals that fool or blunt our immune response. Some even develop “cloaking” technology, allowing them to hide from our immune system. They can drift along almost unseen by our immune surveillance system, which normally patrols the tissues and bloodstream.

A real world example of such successful adaptation has now fully taken root. And we will most certainly regret if we take this one lightly.

### **Why Staph Aureus is Winning**

Our skin is covered with over a trillion bacteria, which generally protect us against the colonization of more harmful microbes. About 30 percent of us carry *Staph. aureus* on our skin right now. Most of us have had or will have *S. aureus* on our skin now or in the future. Before antibiotics, *S. aureus* posed no significant threat to the majority of healthy people.

Microbiologists have marveled that *S. aureus* possesses an arsenal unlike almost any other bacteria. However, the very capacities that strike awe in these scientists now elicit dread among doctors and hospital personnel. *S. aureus* secretes a range of proteins that prepare the human body for invasion, thwart the immune defenses, and invade white blood cells. Most frightening among its defenses is an uncanny ability to make a protein that binds to our own antibodies, fooling our defenses. Because of its many complex proteins, *S. aureus* participates in more varied types of disease processes than almost any other bacteria. This impressive arsenal also means that far fewer *S. aureus* bacteria are required to be lethal than many other bacteria.

It was a chance discovery of mold contamination in a culture surely containing *S. aureus* that led to discovery of penicillin. Herein lay one of medicine’s greatest achievements—the advent of drugs to treat infectious disease. It was this moment that led

to the stunning conquest of many infections of the past and brought about our disturbing vulnerability to infectious disease today.

*S. aureus* once posed its greatest threat to immune-compromised people, such as those undergoing surgery, burn victims, trauma victims, and transplant patients. In this respect, *S. aureus* became the number-one infection in hospitals around the world. But this infection became a growing threat to all hospitalized patients as it developed the tools of resistance.

### **Enter Methicillin-Resistant Staff (MRSA)**

Methicillin-resistant staphylococcus aureus (MRSA)<sup>§</sup>—this is a dreaded term, all too familiar to physicians, nurses, hospital personnel, and all patients who have met its scourge. For decades, *S. aureus* infections were responsive to penicillin. In the 1960s, a synthetic version of penicillin, methicillin, arrived to combat those *S. aureus* strains that were resistant to penicillin. Then, the rebellion began. *S. aureus* developed resistance to methicillin, earning the moniker MRSA. This rebellion was followed by resistance to chloramphenicol, clindamycin, erythromycin, gentamycin, ciproflaxin, trimethoprim, tetracycline, and others.

Today a previously unheralded drug, vancomycin, is the “agent of last resort” for many patients. Vancomycin is not more potent than other drugs. It is a last resort because it fell into less frequent use, so fewer microbes were able to develop resistance to the drug. At least 50 percent of staph infections in hospitals today are multi-drug resistant.

### **MRSA in Everyday Life**

While MRSA can be life-threatening in the hospital, incursions into daily life is what has doctors most alarmed. Robust, healthy men, women, and children have fallen

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<sup>§</sup> The acronym MRSA is now also used to describe multidrug resistant staphylococcus aureus, or those resistant to multiple drugs, not just Methicillin. Thus MRSA could refer to Methicillin-Resistant Staph aureus or Multidrug-Resistant Staph aureus.

seriously ill to this infection. Some have been ravaged and disfigured. Others have died horrible deaths.

### ***Clostridium difficile***

*Clostridium difficile* is the most common cause of infections in the hospital. It is a common bacteria found in the air, water, soil, surfaces, feces, and intestinal tract of humans. In the hospital, these bacteria can be found on hand rails, doorknobs, telephone, stethoscopes, and almost any surface. It normally causes little trouble until the colon is flooded with antibiotics.

As mentioned above, when antibiotics enter the colon, the normal healthy bacteria are dramatically altered, allowing *Clostridium difficile* to emerge from its spore form and take a virulent active state. Almost any antibiotic can trigger the awakening of this dangerous bug, but amoxicillin, ampicillin, cephalosporins, clindamycin, and fluoroquinolones are the most likely to cause trouble.

*Clostridium difficile* is a relative of *Clostridium botulinum*, which makes the most potent toxin known to us (causing botulism). *Clostridium difficile* makes two highly toxic proteins of its own that damage the colon, cause bleeding, and cause diarrhea. More recent forms have doctors deeply worried, because the toxins are even more destructive. *Clostridium difficile* infections often recur, once a person has left the hospital. These later infections are often more serious than the initial infection that develops in the hospital. Ironically, antibiotics are usually needed to eliminate *Clostridium difficile* (though probiotics have been shown to be helpful). In severe cases, surgery is needed.

These bacteria represent just brief examples of bacteria causing severe problems because of antibiotic use. While there are many others, these remind us of the potential dangers in making war with germs.

## **The War on Germs**

There are declared wars and undeclared wars. The war on germs was most certainly undeclared. It grew from noble roots; from treating the very sick, to treating the not-so-sick, to treating those who might get sick. Antibiotics came into widespread use for viral infections, in hopes of preventing secondary bacterial infections—so-called pre-emptive war. It grew from treatment of sick animals into helping animals to grow. Knowing bacteria caused disease in plants, we took the war to the apple and pear tree. As we learned about growing microbial threats, we took the war on germs into everyday life—dish soap, shampoo, toothpaste, and deodorant. Through all this, we did not know that we were training the “enemy.”

Suddenly, though not without warning, we were awash in a sea of microbes with an astonishing ability to resist our most potent drugs and to pass that capability for resistance to neighboring bugs. The casualties of our undeclared war on germs have clearly emerged. *We* are the casualties of the war on germs. There are now hundreds of thousands of tragic cases of individuals who have died from antibiotic-resistant infections. These are surely the casualties we most deeply mourn. But the war on germs now touches all of us directly. It defines our future, should we become weakened, ill, and in need of antibiotic drugs. The past war on germs now shapes our policies, as we decide how to use antibiotic drugs in medicine and in agriculture. It defines how and to what extent we can develop new antibiotic drugs that will be used in the future. It will define the future of medicine.

## **Running Out Of Options**

At a time when the frequency of infections caused by antibiotic-resistant bacteria is rising sharply, the pool of antibiotics in development by drug companies is drying up. Between 1988 and 1992, the FDA approved an average of three new antibiotics per year. Since 2003, that number has fallen to only one approval per year. Moreover, some of the largest drug companies, such as Wyeth, Eli Lilly, Procter & Gamble, Roche, Abbott Laboratories, and Aventis, have either sharply reduced antibiotic research or gotten out of

antibiotic research altogether. A study of the 15 largest pharmaceutical companies and 7 largest biotechnology companies revealed that only **six** of 506 new drugs in development were antibiotics.

According to Joseph R. Dalovisio, MD, of the Infectious Diseases Society of America, “Infectious disease physicians are alarmed by the prospect that effective antibiotics may not be available to treat seriously ill patients in the near future. There simply aren’t enough new drugs in the pharmaceutical pipeline to keep pace with drug-resistant bacterial infections, so-called ‘superbugs.’”<sup>xvi</sup>

Below is a graph of the numbers of antibiotics in approved over the past two decades. It is obvious that the trend is sharply downward. We can contrast this disturbing the rise in antibiotic-resistant bacteria and infection rates.. These trends are clearly in the wrong direction.

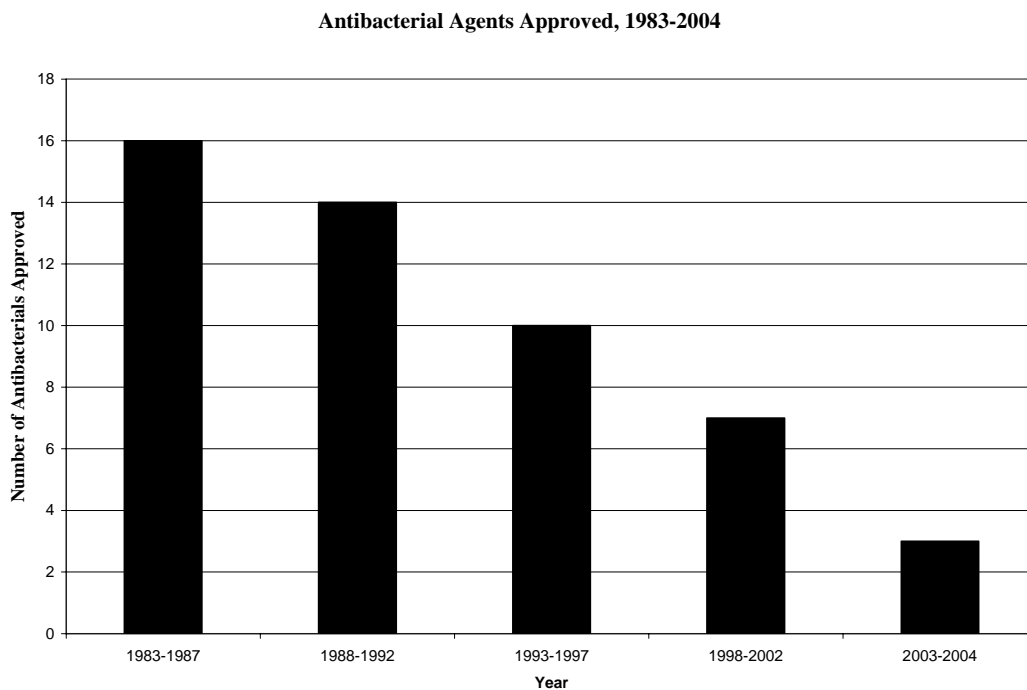


Figure 1.1 The number of new antibacterial agents approved for human use has declined steadily since 1983.

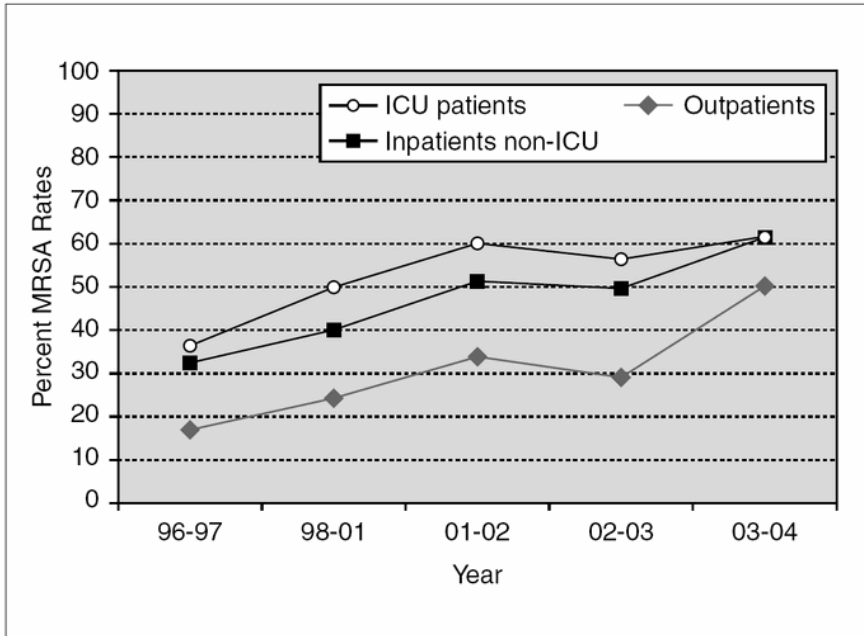


Figure 1.2. Temporal trends of MRSA rates according to data from the NNIS System. MRSA: methicillin-resistant *S. aureus*; NNIS: National Nosocomial Infection Surveillance; ICU: intensive care unit

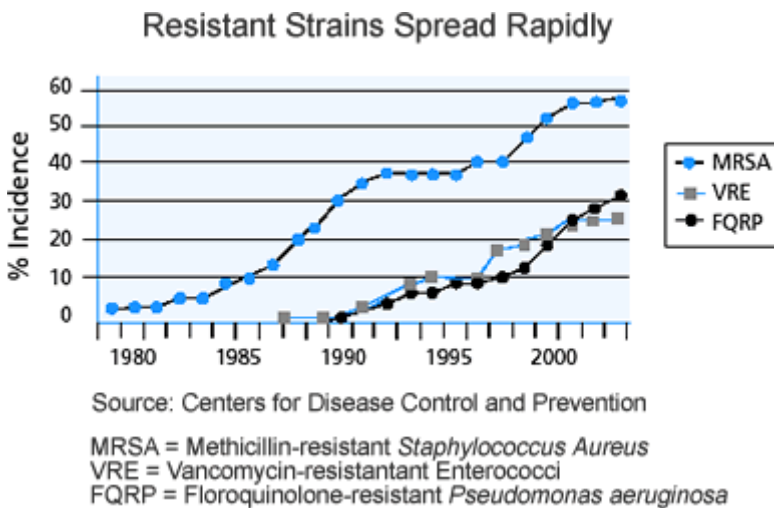


Figure 1.3. The percentage of antibiotic resistant strains of three common microbes has risen steadily since 1980.

The war on germs has led us to a point where there are now infections for which there are very few treatment options. Antibiotic development remains down while research on other drugs is rising. This is largely because pharmaceutical companies have shifted their emphasis to drugs with large markets and to chronic conditions like diabetes, high cholesterol, depression, and arthritis, for which patients must be on long-term

therapy. In short, there is vastly more money to be made from blockbuster drugs than from antibiotics that can only be used sporadically by patients.

## **What Next?**

We have arrived at a fork in the road. Go left, and we are on the path well-traveled. Here, we continue with our focus on killing the microbe and we do so at our own peril. This is the path of emerging infections, antibiotic-resistant bacteria, and few new antibiotics on the horizon.

To the right is the road less traveled. This path holds the same threat—emerging infections, antibiotic-resistant bacteria, and few new antibiotics on the horizon. However, this path is strewn with promising signposts not seen on the path to the left. These messages point to the power of the host, the wisdom of garnering the profound adaptive and defensive resiliency of the human being. The trail to our right has abandoned the microbe-first manner of thinking. While attention to the microbe must remain in sharp focus, our thinking, our research, our treatments, and our core philosophy places the *host* squarely in the center.

Should we choose the path of the host, we begin to marshal a growing body of research that suggests an entirely new way of coping with the microbial world, perhaps even thriving in the midst of our microbe-riddled surroundings.

This path requires that we better understand those things that influence our coexistence with microbes, our defense against them, and our recovery from failed encounters with them. Our discussion now shifts to that path. We become explorers of the complex world of the human and the myriad influences on our cohabitation with the microbes all around.

## **Why Did We Fail in the War on Germs?**

Our efforts at gaining ascendancy over the microbial world have shown impressive individual results, but near catastrophic consequences when taken as a whole. The primary reason for our failure lies with the microbe. They are nearly everywhere and

their ability to adapt is stunning. It was natural for us to perceive ourselves as living in *our world*, where annoying or dreaded microbes occasionally surfaced, to our dread. We have conducted our daily lives oblivious to the untold numbers of microbes around us. How could it have been otherwise? We could not see them. Even the most learned of our scientists encountered microbes largely through microscopes, culture dishes, and gene sequencers.

But our old notion is a fantasy. Microbes, by their sheer numbers, ubiquity, and complexity are the true denizens of this world. We are sharing *their world*. It is estimated that microbes constitute approximately 90 percent of all living matter on this earth.

Professor William Whitman at the University of Georgia has calculated that the number of bacteria in all the nooks and crannies of earth, above and below ground, is an astonishing  $5 \times 10^{30}$ . That number is a little hard to fathom—a five followed by 30 zeros. To put it in some perspective, the number of bacteria on earth is almost one billion times more than the total number of stars in the universe (about  $10^{21}$ , or a 10 followed by 21 zeros).

The Grand Prismatic Hot Spring located in West Yellowstone is highlighted by a hue of extraordinary colors that fade from red, to green, to blue, to purple. These regions of the hot spring are colored this way because of different species of bacteria, such as *Chloroflexus* (green) and *Chromatium* (purple). To put the sheer numbers in perspective, the bacteria in a single three-inch-by-three-inch chunk from the hot spring outnumber the total number of people on earth.

Even the coloration (or discoloration) of some of our most revered ancient paintings owe their look to bacteria. For example, the famous frescoes in the Crypt of Original Sin (Matera, Italy) owe their rosy discoloration to a bacterium known as *Rubrobacter radiotolerans*.<sup>xvii</sup>

Beyond such exotic features as hot springs and medieval paintings, the dirt under our feet is teeming with some one billion microbes in every gram of soil. And this soil is a virtual war zone. In order for soil microbes to survive, they must produce their own antibiotic compounds or they will be overrun by their neighbors. It is an ancient game of chemical warfare carried out invisibly beneath our feet every day.

These dirt-bound warrior microbes are the very same ones with which our children play out in the backyard and the ones tracked beneath our shoes into our nicely carpeted homes. To our benefit, it is exposure to these microbes that helps prime our immune system as we grow up. In many cases, it is the antimicrobial defenses of these dirt-bound microbes that have given rise to some of our own medical antibiotics. With all due respect, soil microbes are our allies.

But these same soil microbes also possess a spectacular, if not disturbing, trait. They literally eat antibiotics for breakfast. Not only can they live off natural antibiotics, but they have even evolved to live off our modern synthetic antibiotics. Scientists have been humbled by the sheer number of bacterial species able to accomplish this feat, their presence in many different soil types, and the large number of antibiotics they can use.<sup>xviii</sup> That bacteria can actually consume antibiotics as a food source expands our concerns well beyond the issue of antibiotic resistance. The fact that many of these antibiotic-loving soil microbes are closely related to human disease-causing bacteria only adds to the dilemma we now face.

We have been living with a comforting (and outdated) notion that we can somehow conquer microbial infections by carefully crafted molecular agents. While our drugs have saved countless lives and future drugs are expected to do likewise, it now seems unwise to frame our encounter with the microbial world as a war. In this chapter, I use the title “Casualties of the War on Germs,” because our approach to infections has been treated as a war. Our terminology has been that of war. Even, our description of the immune system has embraced war metaphors. Indeed, during epidemics in which thousands, if not millions, of innocent people died, it must have seemed like war.

But our war metaphor must now yield to a maturing vision. If we are at war, we are outnumbered by odds so vast that we can surely not win. Consider the virulence odds. It takes only 500 cells of the food-contaminating bacterium *Campylobacter jejunii* to make a person ill. This means approximately 2 organisms per milliliter of a 180-milliliter serving of milk, or about three-fourths of a cup of milk.<sup>xix</sup>

It takes only 200 cells of *Shigella dysenteriae* to bring down a 200-pound man with a bout of dysentery. *Vibrio cholera* takes only 1,000 bacteria to cause illness, while *E.*

*coli* 0157:H7 requires only 10 to 100 microbes. It takes roughly 100 *Staph aureus* per gram of food to produce enough toxin to cause illness. In someone with weakened immunity, the number of bacteria required to cause illness is even smaller.

The botulinum toxin, produced by *Clostridium botulinum* (and associated with a serious form of food poisoning), is the most potent naturally occurring toxin known to humankind. The toxin is lethal at a femtomolar dose of  $10^{-9}$  g/kg, which makes it some 15,000 to 100,000 times more potent than sarin gas. More simply, a single gram (about one-fourth of a teaspoon) would kill more than 1 million people. After the 1991 Persian Gulf War, there were 19,000 kilograms of botulinum toxin produced by the Iraqi regime unaccounted for. This was estimated to be roughly three times the amount needed to kill the entire human population by inhalation.<sup>xx</sup>

If we are not overwhelmed by the potency of bacteria and their toxins, we must certainly stand in awe of the rate at which bacteria can multiply, reproducing every twenty minutes. Their ability to swap genes renders them able to adapt in ways that would ordinarily take millions of years if left to natural processes.

Fortunately, much of the microbial world is of little direct threat to us. Indeed, without most of it, the world of reforestation, soil enrichment, plant growth, and animal life would simply not exist. We are living in a world largely driven by microbes, but we see only the tapestry. We see the web, but we cannot see the weaver.

This leads us to the second reason for our failure in the war on germs, which lies with us—the host, the human being. While the world around us is teeming with microbes, we have only begun to understand the vast microbial world that lies on and within us. Remarkably, the weaver has woven *us* into the web. The microbial threads have been so finely stitched into the fabric of our own bodies that we and our microbial companions behave as one.

**Next: Chapter 2: You're Not Who You Think**

## About the Author

Michael A. Schmidt, Ph.D. did his doctoral research in molecular medicine and biochemistry within the Life Sciences Division at NASA Ames Research Center. During this time, he also did a fellowship in the Psychophysiology Research Laboratory, investigating neurophysiologic and autonomic changes in humans under extreme conditions. He has also studied neuroscience and metabolomics at Lancaster University (UK). Dr. Schmidt is on the faculty of the Metabolomics and Systems Biology Training Program at the University of Colorado (University of Colorado Health Sciences Center). He also teaches in the regenerative medicine program sponsored by the University of South Florida, where he lectures on metabolic networks, systems theory, and clinical chemistry. Dr. Schmidt works closely with the medical and bioinformatics groups at the Manchester Centre for Integrative Systems Biology (U Manchester, UK). He has spent some 20 years in the field of metabolic modeling and pattern recognition related to human performance.

He is currently part of the Space Biomedicine working group at NASA Ames Research Center, focused on developing informatics systems for physiological and medical data applied to human space participants. Through his company Sovaris Aerospace, he also works with the Human Tissue Analogues Group at NASA Johnson Space Center, using 3D tissue models to study human tolerance to spaceflight. In addition to *Beyond Antibiotics*, Dr. Schmidt is the author of *Brain-Building Nutrition: How Dietary Fats and Oils Affect Mental, Physical, and Emotional Intelligence*. Dr. Schmidt is a member of the Society for Neuroscience, the Metabolomics Society, and the Epigenetics Society.

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