

Life as an Infectious Diseases Physician Scientist: Science is Humanity's Lifeline

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My career as a physician-scientist grew out of my desire to address challenges to human health posed by infectious diseases. I went to college at the University of California at Berkeley in the early 1970s. The Vietnam War was still raging, and the assassinations of Martin Luther King, Jr., and Robert F. Kennedy and the horrors of Watts and Newark were still fresh in my mind. In the eyes of a 16-year-old freshman, the world seemed full of inequities and people who did not benefit from the fruits of human innovation and progress. I hoped my education would help me develop tools to make the world a better place for everyone.

I had grown up in a home that valued education and equality, 4 decades before my old backyard became the lap of Silicon Valley. I was oblivious to STEM (science, technology, engineering, mathematics). In college, I studied art history and psychology, disciplines that gave me a perch from which to view how humans have represented history throughout the ages, depicted their identity, fears, and sorrows, and tools to better understand human behavior, differences, and dysfunction. I was particularly intrigued by artistic renditions of the Dance of Death, flagellants, and garbed doctors hoping to protect themselves from their patients, images of people ravaged by plague, cast off, mistreated, and disenfranchised from society. I wanted to learn more about the effects of disease on people and societies. So, as my college education drew to a close, I decided to pursue a career in medicine. I felt medicine would provide me with knowledge and tools that could help improve the human condition. As I immersed myself in premedical classes and learned about Mendel, Pasteur, Jacob, and Monod and others, basic science entered my radar screen for the first time and emerged as one of the most influential pieces of puzzle that would form my career.

When I began medical school in the late 1970s, unbeknownst to me, my contemporaries, mentors, and the world, a new plague, one that would parallel the Black Death on so

many levels, was brewing globally and in our own backyard in the Bronx. As I transitioned from my preclinical courses to the wards, I began to feel increasingly uncomfortable with the state of medical knowledge. It seemed that the very truths I had just learned in the classroom were insufficient to explain the condition of many of my patients as they failed to reveal the cause of their disease or lead us to the right treatment.

This gap in our knowledge deepened further during my internal medicine training at Bellevue Hospital, where more than a quarter of the medical service suffered from a condition that was identified as human immunodeficiency virus (HIV)/AIDS just as I was completing my residency. Taking care of patients with this disease was overwhelming and challenged my sensibilities intellectually and emotionally. Like those who were victims of the Black Death, my patients were young, dying, often alone, disenfranchised, and marginalized. In fact, like victims of plague centuries before, they were dying from a lack of understanding. It was clear that available knowledge could not explain the disease that appeared, progressed, and spread right before our eyes. It was also clear that this disease defied several long-standing tenets of infectious diseases. The edict that all we need to cure an infectious disease is the right antimicrobial agent, a tenet virtually written in stone, simply did not apply to many of my patients. There was often no treatment, and even when there was it didn't work. Pneumococcal infections recurred despite treatment with highly active antibiotics. Pneumocystis pneumonia recurred despite the availability of active therapies. I still have the image of the desperate breathlessness of such a patient in my head. Cryptococcal meningitis could not be cured despite amphotericin and required lifelong treatment. Multidrug-resistant (MDR) tuberculosis surfaced, heralding the antibiotic resistance crisis.

Neither the therapeutic paradigm nor the antimicrobial agents available to us were able to alter the course of our patients' disease. Our inability to treat them effectively, as we watched them wither away and die was a transformative event in my training and led me to pursue a career in research. I wanted to translate what I observed at the bedside into paradigms to help us understand how the immune system affects the pathogenesis of infectious diseases. I wanted to develop

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more effective ways to treat infectious diseases that arise in those with impaired immunity. Therefore, I have focused my research programs on the development of novel vaccines and immunotherapy for infectious diseases, particularly for immunocompromised patients and those with increased susceptibility to infectious diseases.

Although the experience of taking care of patients with HIV/AIDS galvanized my decision to pursue a career in research, becoming a physician-scientist enabled me to integrate clinical observation and scientific inquiry to address gaps in our ability to care for patients with infectious diseases. The centerpiece of my career lies at the intersection of clinical medicine and science. As I mentioned earlier, I did not have a basic science background when I went to medical school. Although I will admit that this made the path forward daunting at times, it was not an impediment. The road I chose was a natural and logical extension of my clinical training in internal medicine and infectious diseases. I felt great excitement as well as a sense of relief upon recognizing that a career as a physician-scientist would enable me to address clinical questions of scientific importance and scientific questions of clinical importance while continuing to broaden my clinical and scientific horizons. The core requirements of a career as a physician-scientist are to engage in lifelong learning and to continuously adapt to and navigate in an environment of change. Although humbling and constantly testing one's mettle, I have found these challenges worthwhile and empowering.

Science is humanity's lifeline. Our field, infectious diseases, provides continuous and enduring examples of this principle. Since my graduation from medical school, the cause of HIV/AIDS was identified, and successful therapy was developed. The same is true for hepatitis C. *Haemophilus influenzae* meningitis was eliminated virtually overnight by a novel conjugate vaccine; vaccines were developed for varicella, zoster, and human papillomavirus (HPV); and we are well on our way to having vaccines for Ebola and Zika virus disease. This short list does not include discoveries that are leading to new therapies and ways of treating infectious diseases even as I write. The discoveries that benefit our patients today owe their origins to advances in thought that began with the scientific revolution and enlightenment centuries ago, culminating in the development of the scientific method and proof of the germ theory of disease.

Today, our field has grown into a global community of clinicians, educators, and scientists. When a crisis occurs anywhere on the planet, the rest of the planet must respond. Even as tools to detect and treat infectious diseases have grown in number and sophistication, gaps in our armamentarium and the ultimate unpredictability of infectious diseases underscore the crucial role of science as a guardian of the human condition.

Science and the ideas, knowledge, and tools it delivers are indispensable for the safety and progress of humanity.

As I reflect on the beginning of my journey long ago as a liberal arts major who wanted to make the world a better place, I feel very fortunate. My career as a physician-scientist has enabled me to contribute to society in many ways, through work as a clinician, scientist, educator, and mentor. It has also given me the opportunity to continue to learn and gain new knowledge and make new friends. However, the greatest treasure my career has brought is the opportunity to support and encourage others in their effort to make inroads in the fields of infectious diseases, immunity, and microbial pathogenesis. Although my own accomplishments and the advances to which I have contributed are very satisfying, what makes my days worthwhile is the thought that my support and encouragement might help others make discoveries that may alleviate suffering and improve human health.

If I had to identify the single most important lesson I have learned from my journey through the history of art, psychology, medicine, infectious diseases, immunology, and microbial pathogenesis, it would be that new knowledge and the understanding it brings drive human innovation and progress. Being a physician-scientist is the ultimate "helping profession"; it affords one the opportunity to contribute to knowledge at the intersection of clinical care and scientific inquiry, a point of natural synergy with the best chance of making the road ahead safer, gentler, and healthier.

Today, just as when I set out on my career path, major challenges loom as we face an uncertain future in so many spaces and places. As we go forth amid these challenges, we must redouble our efforts to ensure that science survives and flourishes. We need astute, creative, thoughtful physician-scientists to address the pressing challenges posed by antimicrobial resistance, malaria, tuberculosis, fungal diseases, emerging and re-emerging viral threats, and restoring and preventing further damage to the microbiome. There is much to do. Our future is bright.

Supplementary Data

Supplementary video featuring the corresponding author is available at *The Journal of Infectious Diseases* online. Provided by the author to benefit the reader, the content is the sole responsibility of the author, to whom questions or comments should be addressed.

Notes

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