

Physician-Scientists: The Bridge between Medicine and Science

Physicians have played vital roles in advancing medical knowledge, and their impact on human health has been substantial. For instance, eradication of smallpox began with the pioneering work of Edward Jenner; Albert Sabin and Jonas Salk developed the polio vaccine and improved the lives of millions of children; isolation of surfactant by John Clements led to improved outcomes in preterm infants; Mike Brown and Joe Goldstein's work on cholesterol metabolism led to unbelievable reductions in coronary artery disease; and the work of Don Thomas and others made it possible for those with failing organs to recover. In fact, more than 50% of the Nobel prizes in physiology and medicine have been awarded to physicians engaged in science.

Physician-scientists represent less than 2% of physicians, and both practice medicine and are engaged in scientific research. As physician-scientists, we are not only drawn to medicine and the clinical challenges of our patients, we are also drawn to the opportunities that our patients' medical problems bring to science. For a physician-scientist, going back and forth between medicine and science is natural and almost necessary. Although the future of physician-scientists (1, 2) and especially those from underrepresented minorities (3) is a subject of debate, concern, and reform (4), our work in medicine and science remains exciting, personally rewarding, and meaningful to society.

PHYSICIANS VERSUS SCIENTISTS

David Pisetsky recently wrote:

The term physician-scientist is one of those compound words that has been created to unite disparate elements. Our language has others: student-athlete, warrior-statesman and player-coach. The hyphen is a convenient way to keep the words together, but the hyphen cannot obscure the inherent contradictions that fight within. At that core, physicians and scientists (just like students and athletes) can be worlds apart. Becoming a physician-scientist demands a union that can take years to forge and is often tenuous and unnerving. The compound words I noted have two interesting features. The first is that each describes a person of action—physician, athlete, warrior, or player—in conjunction with a person of thought—scientist, student, statesman, or coach. The second feature is that the order of the two words seems to matter, and, in all but one case (student-athlete), the action person precedes the thought person (5).

And I think David Pisetsky is right, there are a number of fundamental characteristics that distinguish physicians and scientists (Table 1), including approach to knowledge, cognitive focus, decision making, adherence to accepted standards of practice, expert opinion, response to mistakes, and basis for remuneration. In fact, some of these competing attributes, such as remuneration, serve to separate physicians from scientists and have, unfortunately, reduced the pool of future trainees. However, importantly the following shared values are common between physicians and scientists:

- Vision—clear sense of what one wants to accomplish in this world;
- Integrity—principles of life based on honesty and consistency;

- Dedication—hard work, persistence, and determination to move ahead despite setbacks;
- Curiosity—questions of why and how; and
- Confidence—a belief in yourself that allows one to challenge dogma and take chances.

MOTIVATING EXPERIENCES AND MENTORSHIP

While serving as director of the National Institute for Environmental Health Sciences, I was giving a talk to a lay audience. A mother with a young child asked me when I first thought about becoming a physician-scientist. Without really thinking, I said I didn't make that decision, my mother made the decision for me. And I can tell you that after interacting with a number of powerful people, it's obvious to me that there's no one more powerful than a mother ... especially, a Jewish one from Long Island. But the question was a good one, and stimulated me to think more about motivating experiences, why I went into medicine, and why I decided to combine medicine and science.

In fact, this experience prompted me to not only ask myself that question but engage 19 other accomplished physician-scientists in answering that question (5). While there are a number of remarkable stories I could convey to you about the families, patients, or mentors that helped these physician-scientists decide what they wanted in life, I thought it might be more meaningful to highlight a short story about a high school friend of mine, Larry Grabin. Larry was not my best friend, but he was a good friend. We played sports at school and caroused together on weekends, but most of all, we competed academically. But actually, there was no competition; Larry was much more intelligent than me. Larry graduated first in our class of over 1,000 students, had perfect SAT scores, and was admitted to Massachusetts Institute of Technology early decision.

During Larry's freshman year, he discovered a lump in his right testicle. This was eventually diagnosed as testicular cancer. Unfortunately, the year was 1971 and oncologists had not yet discovered how to cure testicular cancer. The cancer spread, Larry continued to lose weight, and eventually he was not able to keep up. I frequently visited him at school, at his parent's home on Long Island, or at the Memorial Sloan-Kettering Hospital. Beyond our friendship, what kept drawing me back to Larry was his will to live, his intellectual clarity, and his emotional honesty. Toward the end though, even he admitted that cancer was going to take his life.

A few days before his death, I was visiting him in the hospital; Larry looked at me in a dreamy state. Then suddenly, he focused like a beam of light shooting through a lens and told me that he was going to die soon and felt like his opportunities were going to be wasted. Both of us talked about how science was going to explode during the next decade, and that these discoveries would have profound effects on medicine. Larry told me how much he believed in me, how much we meant to each other, and how much he wanted to do but simply could not; then his confabulated dreamy state returned. In those few minutes of clarity, he encouraged and inspired me, and pointed me toward my future.

Mentors play essential roles in the lives of physician-scientists. For me and many of my coauthors (5), it took a village of altruistic,

TABLE 1. ATTRIBUTES THAT DISTINGUISH PHYSICIANS AND SCIENTISTS

Attributes	Physicians	Scientists
Approach to knowledge	Application	Discovery
Cognitive focus	Unique features of a patient or illness	Generalizable principles of a discovery
Decision making	Rapid	Reserved
Adherence to accepted standards of practice	Almost always	Almost never
Expert opinion	Respect authority	Question authority
Response to mistakes	Risk management review	Basis for potential breakthroughs
Basis for remuneration	Efficiency and effectiveness	Creativity and entrepreneurship

thoughtful mentors to guide us through many of our important career decisions. Some of these people were traditional mentors; others were family, friends, teachers, or patients. While all of these encounters and events were quite distinct, these experiences and mentors shared a common phenotype. These encounters were often serendipitous and were notable for a strong emotional and intellectual connection. While our mentors made it clear to each of us that we had lots to look forward to, these accomplished, thoughtful individuals empowered us to chart our own futures without regard to their own personal gain.

ROLE OF ACADEMIA

Physician-scientists contribute to the reputation and success of major academic medical centers, and consequently, academic medical centers should invest in the future of physician-scientists. Unfortunately, as our institutional finances shrink, the costs of physician-scientists become one of the more vulnerable targets to control expenditures. We should resist this temptation, consider our long-term goals, and use multiple streams of revenue (National Institutes of Health, biotech, pharmaceutical, clinical, philanthropy, patent revenue, and state support) to sustain the research enterprise, especially when it comes to supporting our young physician-scientists.

However, given the looming fiscal constraints at the National Institutes of Health and in healthcare, we need to invent new ways to develop the careers of physician-scientists. We have to be more selective, more strategic, more collaborative, and more generous in nurturing the careers of our less experienced colleagues. Only a small percentage of individuals who complete fellowship training should be offered academic positions as physician-scientists. Those individuals should be selected on the basis of their own merit, as well as the strategic and collaborative opportunities that are unique to each of our institutions. Moreover, we need to ensure that these individuals succeed; failure is simply not an option. We need to develop and support programs to accelerate the career development of exceptionally creative and promising faculty early in their career. These emerging physician-scientists should be protected, connected, mentored, and supported scientifically, financially, and emotionally, especially at transition points in their careers (mentored to independent to established to programmatic research). Finally, we need to recognize that great research programs often emerge from

outstanding clinical programs, and physician-scientists should be actively engaged in establishing these clinical programs of excellence. One of the stunning aspects of academic medicine is the codependence of our seemingly distinct academic missions.

CORE CHARACTERISTICS OF PHYSICIAN-SCIENTISTS

Despite our diverse social, economic, geographical, and cultural backgrounds, there are common threads that are shared by physician-scientists. We love our work, are persistent and competitive, and have enough confidence to display our ignorance. We are dedicated to understanding life and fixing others, we think boldly and plan for where science and medicine will take us, and we believe strongly in the common good. And we are entirely dependent on the common good to nurture and nourish our careers. While we strive to enrich the lives of others, each of us has ourselves been greatly enriched by our patients, colleagues, and families.

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Inhaled Dry Powder Mannitol: A Solution for Cystic Fibrosis

Cystic fibrosis (CF) lung disease is characterized by impaired mucociliary clearance, chronic airway infection, inflammation, exacerbations, and respiratory failure in most patients. Pathogenesis is

driven by autosomal recessive mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, which encodes a chloride channel regulating the composition and quantity of airway epithelial surface liquid (Figure 1) (1). CFTR dysfunction is associated with depletion of this periciliary liquid (PCL) layer (2). Since efficient mucociliary clearance requires an adequate volume