A Question from Emilio: Hypotheses, Hope, and the Legacy of Dominick P. Purpura

Stephen G. Waxman
Chairman of Neurology
Department of Neurology and Center for Neuroscience and Regeneration Research
Yale University School of Medicine
New Haven, CT 06510
Rehabilitation Research Center, VA Connecticut Healthcare Center
West Haven, CT 06516

“I am a twenty-five year old boy, tetraplegic for six years after a ski accident. My lesion is at C5. On the internet I saw research about cellular regeneration, and I would like to know if it is possible to give form to my dreams of walking again some day. Looking forward to receiving an answer from you, I remain yours truly, Emilio”

As a scientist, one is taught to be creative and to challenge old ideas, while at the same time to be data-driven and intellectually rigorous, carefully delineating what we know from what we don’t know, what is possible from what might be possible or is not possible. As a practicing doctor, on the other hand, one is schooled in making the most of what we know now, using knowledge—even if incomplete—to improve the lives of our patients. And as a physician, one learns about the importance of giving patients hope.

How can the clinician-scientist marry these endeavors? Is it possible to be data-driven and scientifically critical (“we can’t yet cure your disease”) while at the same time providing hope (“in the future, we will be able to cure your disease”) and, if so, how do we provide as much hope as possible? Most medical researchers receive questions, by mail, by telephone, and by email, from people around the world who are waiting for their diseases to be cured.

The email from Emilio appeared on my computer screen several years ago. Even in a world of rapidly-advancing research, the dilemma was clear: although we are making rapid progress and restoration of function in spinal cord injury now represents, in my view, an achievable objective, it is unlikely that Emilio will walk again within the next few years. What was I to tell him?

As I thought about Emilio and how to answer him, I recalled my own struggles as a 26 year old medical student. I of course was not paralyzed, but the challenges—how to develop into a productive scientist, and a skilled physician? How to meld the two? How to make the combination of professional life and family life work?—seemed formidable to me. In a world of over-worked clinicians, and of scientists making great discoveries one day and struggling to get National Institutes of Health (NIH) grants the next, I felt quite small, and I was not sure where to go for advice.

By chance, or perhaps by destiny, I ended up knocking on Dom Purpura’s office door. The ensuing events, mere discussions between a world-famous brain scientist and a budding clinician-investigator, had an enduring affect on me, and helped to launch a career.

“Come on in, son, would you like some coffee?,” Dom began. And as he listened to me, he said “come on over here, and have a look at the oscilloscope.” After showing me his experiments in progress, spark after spark igniting nerve cells to fire, Dom shared an image of a neuron from a child with mental retardation and epilepsy. And he told me “one day we will cure epilepsy —maybe not me, but perhaps you. How do you think we can do it?.” This was the first of many discussions in Dom’s office, each one welcoming, each one encouraging. They occurred over my five years at Einstein and, at each juncture, as he re-invigorated the Department of Anatomy, as he built up the Kennedy Center, as he launched the Department of Neuroscience, Dom found the time—or made it—to meet with a student, to ask provocative questions, to give invigorating insights, and to share a picture of the future that was always filled with hope.

Years later, as a fully launched scientist and physician, I realized how much my time with Dom meant to me. I did not decide to work on epilepsy—my passions had evolved around multiple sclerosis, spinal cord injury, and neuropathic pain, but Dom’s lessons and his belief that science can help people stuck and propelled me through-out my career. They convinced me that we build good doctors, good scientists, and good clinician-investigators one-by-one, via the type of engaging conviction (some call it role-modeling) that Dom Purpura used so wisely to ignite innumerable careers.

So, what could I write to Emilio? After a few days, I replied “Dear Emilio, I was sorry to hear about your injury, and I appreciate your writing. I can’t tell you when, but I can tell you that a small army of talented, energetic scientists are working around the world in an effort to restore function—maybe not enough to dance like a bal-
lerina, but well enough to be able to take some steps—in people like you. I don’t know when, but I’m confident that we will win the battle against spinal cord injury.”

I do not think I could have responded to Emilio had I not learned, from Dom Purpura, the importance of humanity, of encouragement, and of hope, in science and medicine. I think that Dom was watching over my shoulder as I replied to Emilio. I know that Emilio’s message was important for me, for I share it with my students, with the entreaty that they should find their own Emilios, who can help propel them toward cures for mental retardation, diabetes, cancer, or Lou Gehrig’s disease. And I know that each student I mentor is a tribute to Dom Purpura and the lessons that he taught me.

Over the past five years my co-workers and I have worked out, for the first time, the molecular basis for a human hereditary pain disorder. It is called erythromelalgia, and it is an autosomal dominant disorder known to be caused by a sodium channel mutation that causes nociceptive neurons to shriek when they should be silent. This is characterized by searing pain in the hands and feet in response to any warmth and it can be very disabling. We now understand, in exquisite detail, the genetic basis for this disorder. And we understand the gene product, what it does within nerve cells, and how it causes pain. I received another e-mail, in the context of this work, a few months ago. It said,

“Dear Dr. Waxman, I just read about your research on erythromelalgia and was most interested in it. My daughter has erythromelalgia. She is fifteen and nothing treatment-wise has helped. She has had to give up playing sports and cannot go to the mall or do most things that a teenager would like to do. I hope you continue to work at finding a cure. Thanks, ------’s Mom ”

How can one thank someone for a note like that? I sent a reply by e-mail. Again with the sense that Dom was watching. Then I went to the lab. To try to find that cure. And I know that Dom was watching over my shoulder, even smiling. It is incredible how tight a bond we develop with the people who teach us, and with the people we serve.

Although I largely live in a world of genes, ion channels, and nerve cells, I find myself shuttling back and forth between molecules and man, between hypotheses and hope. And so I answer the e-mails from patients and their loved ones. I have learned that this is part of the responsibility of the clinician-scientist. And I have learned to cherish it. This is something that I learned from my heroes. It is part of the enduring legacy of Dominick Purpura.