Leading by Example and Design: The Joseph St Geme Jr Leadership Award, 2016

David K. Stevenson, MD

abstract

Leadership begins not by being out front or within a team but by first learning how to follow someone else and then trusting them to lead you with your best interests at heart. Indeed, most leaders are following the direction of some other person or group of people; for example, a chief executive officer reports to a Board of Directors, and a university president reports to a Board of Trustees, or at least they follow the advice of other people who might offer them wise counsel. Such nascent leadership thus entails deciding whom to follow, which means being a good judge of people. For some, the ability to judge other people seems to be innate, but it can also be learned by observing leaders making decisions and witnessing the consequences of their choices and actions over time. As an undergraduate at Stanford, I met John D. Goheen, professor of philosophy, who served as chair of the Department of Philosophy in the 1950s. He was a student of Alfred North Whitehead at Harvard, steeped in the teachings of 1 of the most challenging thinkers of the 20th century. Whitehead was a mathematician and philosopher. His "process philosophy," for which he is best remembered, describes the world as a network of processes of which people are an integral part.[1] His thought reflects the importance of process and connectedness (reality is a web of processes) and thus changeable environments, or contexts, for successful decision-making in the world. Applications of his thought exist in many fields, including the physical and life sciences, but also in the social sciences, particularly education.

John Goheen, evolving his own thought from Whitehead's innovative philosophical musings, taught me that logic can prove things, but it cannot invent them. He observed that imagination is as critical to paradigm-shifting philosophy or science as analysis. John recognized the need to create novel contexts for learning and created many of the unique advising and educational programs at Stanford over the next 20 years, which encouraged students to learn and live on their own terms, to take intellectual risks, and to not fear failure. He helped create the mutable structures and processes, the changeable environments, where Joe St Geme Jr thrived as an undergraduate, along with many future business leaders of Silicon Valley and so many others. He led by example, but he also "led by design," which reflected the teachings of his mentor about the importance of contexts, even for individual successes. Bill Barnett, professor of business at Stanford, says, "When you lead by design, your job is not to know the future but to create an organization that discovers the future. Leading by example shows the way, but leading

Stanford University School of Medicine, Stanford, California

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Address correspondence to David K. Stevenson, MD, Department of Pediatrics, Stanford University School of Medicine, 1265 Welch Rd, Room X157, Stanford, CA 94305. E-mail: dstevenson@stanford.edu

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by design creates a system that discovers the way" (http://www.barnetttalks.com, Barnett Innovation by Design Webinar 2015).

My father, John K. Stevenson, professor of surgery at the University of Washington, also led by example. He was a "surgeon's surgeon," but I was not going to be one. Nonetheless, he also led in that other way: He led by design. Indeed, some of his students did become some of the first pediatric surgeons, but for many others, he created learning environments that encouraged them to pursue their own dreams of how as doctors they might improve the lives of others. Thus, he led in both ways. This is what he also did for me. I did not follow his example and become a pediatric surgeon, but, by his design, I was able to find my own way and became a pediatrician and neonatologist.

At Stanford, I joined 2 colleagues who also led by example but were committed to creating an environment conducive to innovation and discovery, Drs Philip Sunshine and Ronald L. Ariagno. They, along with Dr John D. Johnson, my research mentor, taught me that risk taking in medicine was best undertaken through experimentation in which minimal or reasonable risks could be assumed and the knowledge obtained could be generalized. Moreover, the message became clear: Leading by example was not enough, and leading by design was even more important for innovation and discovery. Phil Sunshine also taught me that critics would be my best friends, and at the same time, he reminded me of why I should do more than research, that I should apply what I learned to change practice and unite academic and private practice neonatologists in a common effort to improve the health of mothers and babies. Subsequently, I helped create new organizations: the California Association of Neonatologists (https://canneo.groupsite.com/main/summary) and the statewide quality improvement networks: the California Perinatal Quality Care Collaborative (https://www.cpqcc.org) and its maternal counterpart, the California Maternal Quality Care Collaborative (https://www.cmqcc.org). These organizations introduced a new statewide culture, structures, and processes and created a new paradigm for public maternal and child health improvement.

On a more personal note, I would like to provide 1 more example of leading by design. This academic story begins with a singular focus on a protein, heme oxygenase-1 (HO-1), the first and rate-limiting enzyme in the catabolism of heme. The porphyrin ring is one of the oldest organic molecules on Earth, and it probably arose in the prebiotic era. Living organisms use porphyrin rings by complexing them with catalytically active metal ions. Heme is such a metalloporphyrin and also known as iron protoporphyrin IX, regardless of the oxidation state of the chelated iron. The biosynthesis of heme is essential to the metabolism of many living organisms on Earth, so its biosynthesis is controlled by a large number of enzymes. As heme biosynthesis is essential to much of life on this planet, so is its degradation, and this latter phenomenon has been and still is the main focus of much of my research.

Until recently, I was focused mainly on the toxic effects of this pathway, introducing a variety of technologies to monitor the production of bilirubin[2] or to control that production[3,4] but also new ways of using light to eliminate the pigment.[5,6] Nonetheless, there are important beneficial effects of the pathway that also need to be considered. The bilirubin–bilirubin shunt helps maintain the redox state of every nucleated cell.[7] Carbon monoxide is an important signaling molecule and can mediate vascular relaxation through a variety of mechanisms, stimulate angiogenesis, and inhibit inflammatory cytokines, and it generally has antioxidant, inflammatory, and antiapoptotic effects.[8] Such consideration led me to study HO-1 expression, immune cell type-specific signaling, and spiral artery remodeling, among other things. Because the relative inability to upregulate HO-1 in response to a stressor such as pregnancy is associated with anomalous immune cell type-specific signaling or classic (M1) proinflammatory activation of macrophages,[9] it can, in turn, lead to the failure of vasculogenesis and immune tolerance, and thus abnormalities of deep placentation (at least in the mouse), as can be dramatically visualized in a casting of an HO-1–deficient mouse placenta,[10] but it also just might be contributing to the great obstetric syndromes, including premature labor, all of which have also been associated with failure of transformation of the spiral arteries.[11] My singular focus on the protein HO-1, important to be sure, had morphed into a scientific adventure to discover the causes and find new ways to prevent a complex human condition, preterm birth.

A little over 5 years ago, at the request of Dr Michael Katz and the March of Dimes Foundation, I was asked to establish and lead, or lead by design, a transdisciplinary center to study preterm birth.[12] I am now working with teams of scientists from many different disciplines, like scientific detectives, looking for clues to solve the mystery of preterm birth. We are not afraid to fail, each false lead or technical difficulty giving insight into a change in direction or a technical improvement in our quest. For this purpose, we are taking an integrated approach for a system-wide analysis of term and preterm pregnancies with many different areas of inquiry. Our goal is to create an integrative personal omics profiling of pregnancy, to describe pregnancy

from many different perspectives simultaneously: biologically, clinically, and sociodemographically. We are introducing new technologies for this purpose, allowing us to study the temporal variation of the cell-free RNA transcriptome during pregnancy, explore a new way of dating pregnancies, and identify anomalies in gene expression that foretell pathologies of pregnancy.[13] We are using mass cytometry of time of flight mass spectrometry to provide not only better phenotyping of immune cells but also the characterization of their signaling behavior in pathologies of pregnancy.[14] We are also characterizing the microbiome to identify unique community-state types associated with preterm birth, such as the diverse type IV.[15] And we are using a variety of novel computational approaches to describe our findings, sometimes visually simple ones such as Markov chain analysis, and other computational approaches that are dauntingly complex. We have created structures and processes to ensure the connectedness of scientists from disparate disciplines and new changeable environments conducive to innovation and discovery.

Let me conclude with the admonition: Lead by example, and lead by design. Create contexts, changeable environments, for innovation and discovery. Accept that process is reality, a generational echo of a 20th century philosopher's worldview. Remember that crazy ideas are only crazy until they are not, and the latter transformation may be an indication that there has been a paradigm shift. Understand that failure is on the same path as success.

ABBREVIATION

HO-1: heme oxygenase-1

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