

## American Pediatric Society's 2012 John Howland Award Lecture: pediatricians should be the model for the convergence of science and medicine

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*This lecture was presented at the 2012 Annual Meeting of the Pediatric Academic Societies, Boston, Massachusetts.*

I offer my deep and heartfelt appreciation to President F. Bruder Stapleton and the Council of the American Pediatric Society (APS) for selecting me as the 2012 recipient of the John Howland Award. This is an extraordinary and humbling honor that will stand as the acme of my life and career in academic pediatrics. I want to also thank Ms Brenda Peat, APS executive secretary, for her wonderfully caring support and assistance in the numerous planning events that led up to the annual meeting of the Pediatric Academic Societies.

Dr Stapleton opened the awards ceremony with his important and moving presidential address entitled "Mind the Gap" that called attention to the impact of disparities on child health and the future of pediatrics. Needless to say, I am incredibly indebted to my wonderful colleague, Dr David Stevenson, past president of the APS and currently the vice dean, senior associate dean for Academic Affairs, and Harold K Faber Professor of Pediatrics at Stanford. Dr Stevenson's very memorable, albeit deeply embarrassing introduction and personal portrait of me, was delivered with great skill and well-placed humor at the award ceremony and is memorialized in his "introduction" that accompanies this article. I note in passing that the endowed professorship held by Dr Stevenson is named in honor of Dr Harold K. Faber, who was the last member of the Stanford faculty to receive the John Howland Award. This occurred in 1956, 4 y after this important honor was awarded to its first recipient, Dr Edwards A. Park of Johns Hopkins School of Medicine, 60 years ago. Of note, Dr Howland had served as chair of pediatrics at Johns Hopkins and the Harriett Lane Home from 1911 to 1926 and is considered a founding father of academic pediatric departments.

At this year's award ceremony, what may become a new tradition began with a presentation by a member newly elected to the APS. This presentation entitled "Childhood Adrenocortical Carcinoma: Lessons Learned from a Rare Malignancy" was delivered by Dr Carlos Rodriguez-Galindo, associate professor of Pediatrics, Harvard Medical School.

Dr Wanda Barfield, director, Division of Reproductive Health at the Centers for Disease Control and Prevention, gave another exceptional presentation that preceded my own address. Dr Barfield is 2012 recipient of the Norman J Siegel New Member Outstanding Science Award that honors the memory of Dr Siegel, a beloved leader in American pediatrics. Dr Barfield's presentation was entitled "Beginning With the End in Mind: Social Determinants and Disparities in Perinatal Health." Without question the future of pediatrics and child health of our nation and the world is in the hands of individuals like Drs Rodriguez-Galindo and Barfield, along with the remarkably talented members of the APS, the Society for Pediatric Research, and the Pediatric Academic Societies. The future is with you.

I would like to begin, rather than end, my presentation thanking my wife and life partner Peggy Daly Pizzo. Nearly everything I have learned about life, integrity, resilience, and the importance of children in society emanates from our relationship that soon will be five decades long, which started with a blind date and which has continued in an ever more luminous relationship to the present. Yes that means we were children, or at least adolescents, when we began our personal and professional journey, a perfect start to a pediatric partnership. Sadly, a recurrence of a medical problem prevented Peggy from attending the award ceremony as planned—a great sadness for both of us and our family and friends.

Peggy and I are the personal beneficiaries of two wonderful daughters. Dr Cara Barone is also a Children's Hospital, Boston-trained pediatrician and practices pediatrics in Palo Alto. Cara is here today and her husband, David Barone, is looking after their two children, Ryan, who will soon be 5 years old, and Lucia who just turned 3. Our second daughter, Tracy Frey, is a Stanford MBA and is currently a "Googler" in Silicon Valley parlance. Her husband, Paul Frey, and their nearly 2½ year-old son Silas are with Tracy in California, since she is in the last weeks of pregnancy. Between Cara and Tracy we have three and soon, we hope, four grandchildren, which is a wonderful blessing. I also appreciate my brother Michael and his wife Diane, who traveled from New York to attend this event.

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Received 1 June 2012; accepted 4 June 2012; advance online publication 25 July 2012. doi:10.1038/pr.2012.83

In addition, I offer thanks to Chip Brienza, our good friend of many decades, for making the journey from Washington, DC, to Boston. I am also very pleased that my executive assistants from Boston and Palo Alto, Sharon Olsen and Mira Engel, who have enabled me to work successfully for more than 16 years between them, are here today for this event—their support is deeply appreciated and valued in ways that I cannot even begin to describe or delineate.

I should add that my soon to be 92-year-old mother very much wanted to be here for this very special event. I'm sure if she was in attendance, she would have told me to get a haircut, which I did, but she would also likely have told me to use that "Grecian Formula on my hair," which I obviously did not! After all, since this is a lifetime achievement award, the graying that accompanies the passage of years is at least some validation for the years spent living, albeit not necessarily a measure of success *per se*. While I am honored to be receiving the Howland Award for lifetime achievement, I also recognize that most all of my professional achievements have already or soon will recede into the sands of history.

Although not often apparent at the formative stages of careers in medicine and science, it generally becomes increasingly clear over time that our most enduring legacies are reflected in those who succeed us—our families, the children and families we have cared for and served, and the individuals we have educated, trained, and learned from over the years. We are reflections of those who taught us. I was inspired to pursue pediatrics by Dr Robert Haggerty, who was the chair of Pediatrics at the University of Rochester School of Medicine when I was a student. Dr Haggerty was the 1998 recipient of the Howland Award. I was also guided in medical school by my research advisor, Dr Stan Friedman, working on defining the relationships between stress and infection—perhaps a harbinger of my life in academic medicine. I also want to acknowledge Dr Elizabeth McAnarney, past president of the APS (2004–2005), who was a teacher early in my career, and who subsequently succeeded Dr David Smith (also a former teacher in Boston) as the chair of Pediatrics at Rochester.

Academic careers often do not follow a set script and mine is no exception. In fact, when I graduated from medical school, I planned a career that would focus on community pediatrics, largely in the tradition of Dr Haggerty. That plan changed in unpredictable and unanticipated ways when I entered my internship at the Children's Hospital, Boston, under the guidance of Dr Fred Lovejoy. Dr Lovejoy served as "chief resident" to generations of trainees and I spent time learning pediatrics from him as well as spending some of our 132 h of "on-call in-hospital" time doing research on unexplained fevers in children. I must also acknowledge Dr Bill Berenberg, professor of Pediatrics at Harvard, one of the most amazing physicians I have ever known, along with Dr David Nathan, past physician-in-chief at the Children's Hospital, Boston and chair of Pediatrics at Harvard and 2003 recipient of the Howland Award, who was my first "visit" at the Children's Hospital, and the gold standard for a career as a physician–scientist. Of course there were dozens and

dozens of others, many who contemporaneously accompanied me on this journey and many who are here today, to whom I am deeply indebted.

I doubt my lifetime experience or impact is unique. While I have benefited from colleagues and teachers, I have learned the most from the children and families with whose care I have been entrusted, and I have been most inspired by their inner strength and courage. Individually and collectively, they have revealed the impact of serious illness on pediatric organ systems, families, and society. Their challenges posed the research questions we pursued, and the advocacy positions that needed to be taken on their behalf. Caring for children with complex disorders like cancer, AIDS, and other chronic illnesses poignantly illustrates what works well in our society but also underscores the many challenges, discords, and disparities we still face in pediatrics, both locally and globally.

Children and their parents have taught me about courage and resilience in ways that transcend time and space and that can mute issues that seem to loom large in our lives and which often need perspective. When facing tough issues or problems I think of Ted, who at 10 years of age developed aplastic anemia. After his diagnosis, Ted spent the next 8 years of his life in an isolation room about the size of a modern bathroom that had been designed to protect him from infection and which thus restricted access to anyone not wearing masks and gowns or contact with anything carrying potential microbes. Despite these incredible limitations, Ted found ways to figuratively rise above physical barriers, demonstrating his deep inner strength and drive for life that we have the privilege to observe in children and teenagers. I learned a tremendous amount about chronic bone marrow failure from Ted—although not enough to save his life from a now preventable complication of iron overload. This too is another reminder of the limits of knowledge at different points in time. More than medical and scientific knowledge, Ted and his family taught me about the wrenching impact of a chronic life-threatening disease on a child who is becoming a teenager and young adult. His long illness revealed the impact of disease on siblings, parents, family, and community. This unique experience of caring for Ted has had a lasting impact on my research career and, more importantly, on me personally in ways that transcend words.

I remember Elizabeth Glazer, who lost her life to transfusion-acquired AIDS but whose commitment to her children, first Ariel and then Jake, empowered her to devote her all-too-short life to fostering research and advocacy for pediatric AIDS. Ultimately her advocacy saved the lives of many tens of thousands of children around the world. She and others like her exemplify the power of parents whose commitment and resolve shapes the future for children. We have all experienced parents who put the health of their children before their own. For Elizabeth it was the children of the world that she put first and foremost. Individuals like Elizabeth move us from simply being physicians and scientists to becoming advocates for change. Elizabeth transformed my work as a public spokesperson for research, equality, and human dignity.

I think of Ginny, who overcame a presumed death sentence when she was diagnosed with metastatic sarcoma. Few thought she could survive, but she and her family never lost hope and she lived to become a teacher and mother. Ginny also reminds us of the consequences and the limitations of our knowledge as we configure new treatments, only to find decades later that they can lead to unexpected complications, such as second cancers and life-long organ damage, all of which Ginny has experienced. Despite these challenges, she has continued to find courage and resilience—again, inspiring us to do more and to seek better solutions.

As with Ted, Elizabeth, and Ginny, I recall the faces of thousands of children, adolescents, and families, many who lost their lives, but all of whom participated in research protocols so that future generations of children might benefit from the dedicated work of pediatric investigators and the teams of nurses, social workers, psychologists, pharmacists, and others who refused to accept that nothing could be done. Pioneering leaders like Dr Lori Wiener, co-director of the Behavioral Science Core and head of the Pediatric Psychosocial Support and Research Program in the Pediatric Oncology Branch of the National Cancer Institute, has inspired me because of the work she and her colleagues have done to help children and families cope with the challenge of serious illness. Many of these individuals, including many of my former trainees, are present today and I am grateful for all they have contributed to pediatric science, medicine, and humanity.

For the decades that I was at the National Institutes of Health (NIH), I made it a habit to always walk through our inpatient facility each night before going home. I did so purposely to reconnect with our care team and staff, and to remind me of our shared goal of seeking solutions to horrendous medical problems. Such experiences compel us to put our own personal problems into perspective and to reprioritize around what is really important—the lives of the children and families we serve.

Being an academic pediatrician has been an honor and privilege. I often tell our medical students that even decades later, I feel like I have never had a job or gone to work in the traditional sense of the words. Each phase of the journey has been filled with wonderment, exhilaration, and surprise. While my role as pediatric academician always seemed clear to me, I admit to struggling with an identity crisis when I became dean at Stanford just over 11 years ago. My then-new career path seemed unanchored to my prior decades in pediatrics, until I realized that a not insignificant part of my day job was dealing with temper tantrums and adolescent rebellion—albeit in adult faculty who occasionally masqueraded as children. Who would have thought that a prerequisite for being a dean was first being a pediatrician?

Looking back over the decades of my own career gives evidence of the extraordinary progress that has come from pediatric-related researchers who are members of the American Pediatric Society and Pediatric Academic Societies. They are an affirmation of the importance of basic research and its eventual application to clinical medicine—and show why investments

in biomedical research are so critical. Dr Peggy Hostetter (1), professor of Pediatrics and director of Infectious Diseases, Cincinnati Children's Hospital, poignantly captured some of the highlights of the changes over 200 y in her article. Based on my personal chronology, which is just a few years (more or less) older than when the first Howland Medal was awarded in 1952, a few personal examples help make the point.

- A number of the bacterial and viral infections that dominated the earlier phases of my life and career and that caused fatal or life-long consequences in children have been virtually eliminated by vaccines pioneered by pediatric investigators. I was a young child when polio was still a problem and I was among the cohort first vaccinated in 1954—just a year after Watson and Crick had published their seminal paper on the structure of DNA. When I trained at the Children's Hospital in Boston in the early 1970s, *Haemophilus influenzae* meningitis and pneumococcal diseases were everyday events. But when I returned to Children's in 1996, after a 23-y interlude at the NIH, and when my daughter Cara was beginning her internship at that same institution, *H. influenzae* meningitis and invasive disease was virtually gone, thanks to the work started by Dr David Smith (who was also among my early teachers and mentors) and his colleagues in Boston who continued this work when he moved to Rochester as Chair of Pediatrics. Largely because of vaccines, the worldwide childhood mortality has declined from 20 million per year in 1960 to <8 million in the last couple of years. Remarkably and sadly, despite this progress, we are challenged today by irresponsible fear-mongering and falsified attribution about vaccine safety (perhaps most egregiously the false claim that vaccination is linked to autism) that has left too many children unnecessarily vulnerable to preventable infection(s). Advocacy in pediatrics not only includes support for research, education, and patient care, it also requires us speak out for professional and scientific honesty and integrity that protects children now and in the future.
- During my career, I have had the privilege of watching what were once untreatable cancers now become essentially curable through breakthroughs in basic research, coupled with a national network of clinical trials in pediatric oncology. My good friend Dr David Poplack, director of the Texas Children's Hospital Cancer Center and professor of Pediatrics at Baylor School of Medicine, along with many of his trainees and colleagues around the world, has made survival for children with cancer one of the greatest success stories of biomedical and translational research of the past decades. But, as noted by my description of Ginny, many survivors of childhood cancer suffer long-term complications that accompany them into adulthood. Indeed, survival of childhood cancer is just one example of the rapidly evolving challenge of providing transitional care to adults who are survivors of one or more childhood illnesses.

- When I began my training in pediatrics, the body weight and gestational age of a premature infant was much more than what it is today. Indeed, the ability to treat newborns at gestational ages and body sizes once unthinkable has become commonplace, but the precipitating factors of prematurity, with its multidimensional biological and societal causes, remains all too unabated. Without question, the incredible work of Dr Mary Ellen Avery, the 2005 Howland Award recipient, whose research helped elucidate the cause of respiratory distress syndrome and paved the road to surfactant therapy, has changed the outcome of prematurity in remarkable ways. The pioneering leadership of Dr David Stevenson, who spoke earlier on my behalf, has helped define the field of neonatology and save the lives of newborns throughout the United States and world.
- Although it has taken more than 15 y since the *CFTR* (cystic fibrosis transmembrane conductance regulator gene) was sequenced with high expectation for clinical impact, and while the G551D mutation of *CFTR* occurs in only 3–4% of children with cystic fibrosis, the recent discovery of the beneficial impact of Ifacafort (also known as Kalydeco or VX-770) has offered hope that genomic-based therapies could be on the horizon for some serious pediatric diseases, especially when investigators and industry (in this case Vertex Pharmaceuticals, Cambridge, MA) are focused and committed to overcoming serious illness in children. Similar persistence by pediatric physician–scientists is permitting a rise in gene therapy in hemophilia and other disorders and in helping to define the future promise of stem cell biology and regenerative medicine.

These are just a few examples among many other advances and challenges that are transforming the future health and well-being of our children, now and into the future.

Although many of the fundamental and clinical discoveries of the past decades have been startling, including some illustrated above, all too many children suffer from the consequence of poverty and societal forces leading to hunger, malnutrition, and environmental toxins contributing to asthma and respiratory illnesses. The important issues of health disparities in children was featured in Dr Bruder Stapleton's presidential address and in the very thoughtful presentation by Dr Wanda Barfield on receipt of the Norman J Siegel New Member Outstanding Science Award. Although global poverty has declined from 50% in 1981 to 22% in 2008, this is still a distressing and unacceptable number. In developing nations many individuals are living on the equivalent of \$1.25 cents per day. Moreover, there is an ever-widening economic gulf in our nation that is leaving all too many children and adolescents with blunted hopes and deflected aspirations. As pediatricians, we have long known that the complex interplay between biology and psychosocial forces in disease—and the widening gap between those with resources and those without—is notable and significant. In the end, socioeconomic deprivation, violence, and accidents impact more children than the diseases that have occupied most of our

attention and careers. They too require our focused attention and pursuit, as was suggested by Drs Stapleton and Barfield.

We are at the threshold of enormous change in the United States and worldwide in health and health care, and pediatricians have a unique and important role to play in seeking solutions. But this will require change in our profession, focus, locus, and expectations. The role of the pediatrician continues to need redefinition and, in tandem, so does the focus of training programs as well as the institutions that train and educate current and future members of our community. This is part of a bigger issue that is impacting all of medicine but one where pediatricians can play an important and leading role, if we have the courage and resolve to do so.

The rising cost of the current health-care system in the United States is unsustainable. Our nation spends more than \$2.6 trillion per annum on health care, which now consumes more than 17.6% of the gross domestic product. The continuing rise in health-care costs cannot continue. The employer-based fee-for-service model in the United States contributes to these expenditures, driven by technology, drugs, procedures, and expectations for care. Patient care has become highly fragmented and increasingly impersonal. While many in our society believe that health-care reform is needed, there is wide disagreement about what the health-care model should be, how it should be funded, and who should deliver it. Here is where the role of pediatricians can be transformative, not just for children but also for the renewal of our entire health-care system. Let me offer a few examples and reasons:

- Pediatricians have long understood, indeed first defined, the nature of the medical home, which needs to be a family home. Pediatricians now need to define new models of care that focus on promoting healthy children as a prelude to their becoming healthy adults, thus switching the medical model from disease management to the promotion of health and well-being. They also need to create and develop high-quality patient-centric care that is much more cost efficient. Furthermore, pediatricians need to help lead the transitions in care that take place as children with chronic childhood disorders become adults. Some of these health transitions have already taken place (e.g., children and teenagers with cystic fibrosis or adult congenital heart disease). Other medical conditions, especially neurodevelopmental disorders of children, represent more difficult challenges and need new models of care to enable assimilation and successful transition from pediatric to adult care providers.
- The promotion of child health should be delivered in a team-based model. The unique role of the pediatric-trained physician should be particularly focused on complex chronic disorders as well as research, education, social and health policy, and advocacy.
- Pediatricians should help develop and use the tools that define the biologic risk of disease before birth down to the embryo level as well as during childhood. They should also play a key role in helping to delineate the biological, environmental, and psychosocial risk



factors that contribute to chronic diseases in adults that could be impacted in children. Clearly, these approaches will pose a number of ethical and societal issues and pediatricians should directly contribute to those discussions.

- Lifestyle contributors to chronic disease morbidity begun in childhood will require new collaborations of pediatricians with social scientists, psychologists, early-childhood education specialists, and others. While we have recognized the public health problems of childhood obesity and its consequences throughout the life cycle, we need new interdisciplinary approaches to address this and other biopsychosocial issues more assertively and successfully. Similar approaches apply to addressing the environmental causes of disease through collaboration and cross-fertilization of medicine with leaders in environmental and social science. This may mean the creation of new domains of expertise and specialization by future pediatricians.
- Because the future of pediatrics is increasingly interdisciplinary, the education of future pediatric leaders will need to transcend the walls of traditional programs and children's hospitals. Free-standing children's hospitals have defined the care of children and the training of the pediatric workforce for over 150 years, but they now risk becoming too isolated from a future that requires closer integration with the broader university complex along with new synergies and cross-fertilization. If we are not proactive, "free standing" could come to mean "standing in isolation," which is not good for the future of children.
- The focus of "primary care" should be on chronic and complex care, and the well child-care role of pediatricians should be coordinated through team-based management. This will require changes in training programs and in the expectations of physicians, parents, payers, and more. It will also require new and as-yet-undeveloped modes of communication that will employ information technology and telemedicine in unique and different ways that can be remote, but which will also need to be hands-on. The primary care specialist and the pediatrician will need much more grounding in genetics and predictive medicine and informatics. They will also need greater awareness of companion disciplines in the social sciences, education, and business.
- There is still a need for pediatric specialists, but some of these will coordinate care via teams of physicians and other providers in addition to providing direct care themselves. Regional networks caring for populations

of children will require new levels of interaction and coordination. Population sciences from biological risk factors for disease to epidemiology, biostatistics, informatics, and health policy, to the creation of new models for health-care delivery and wellness preservation will feature prominently in this new order.

- Of course, training and educating a new cadre of physician-scientists and physician-scholars are essential if we are to create a better future for children. We need pediatricians who focus on basic science as well as clinical and translational science, population health science, and the emerging fields of care delivery and regulatory science. Within this, we need a cadre of pediatricians with new skills in social science, education, engineering, environmental science, ethics, and business. The opportunities are vast, as are the challenges. The pediatric community and APS should foster new models of education and training that shorten the length of training, create tracks that optimize the outcomes, and create greater opportunities for success and leadership, particularly for women and under-represented minorities.

It is all too easy to stay in our comfort zones and continue to think of pediatrics as we have known it through the present. I fear that would be a serious mistake. The next several years will be particularly fiscally constrained in the support of research, the social safety net, and payments to physicians and hospitals. Medical schools and medical centers will struggle unless they have clearly defined their missions and goals, and focus on the coordination of innovation and discovery in education as well as new approaches to clinical care. Pediatrics should lead the future, but pediatrics must also become a part of the whole and not just the first phase of a complex, lifelong journey.

I have been privileged to be a member of the academic community and the APS. I view my own role as minor in comparison with the giants who have helped to create the world as we know it today—a number of whom I have been honored to count as teachers and role models, including a significant number of previous Howland awardees. I stand in their shadows. I offer my gratitude, appreciation, and deep respect to all of these past and current leaders. That said, my hope lies with the future generations of academic pediatricians who will help change medicine and science in ways that we haven't even yet discovered and who formulate solutions to the unknown. The future of children, and, as a result, society, rests with you. Good luck and thank you.

#### REFERENCE

1. Hostetter P. What we don't see. *N Engl J Med* 2012;366:1328–34.