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I have spent my career trying to minimize vaccine-preventable disease burdens through enhancing the use of available vaccines including helping to develop recommendations for vaccine use and ways to maximize uptake of those vaccines in populations for whom they are recommended.

I grew up in The Bronx, New York. My first remembrance with regard to vaccines took place in 1955 when I was in second grade. The Salk polio vaccine was licensed and I was not too thrilled to be getting a “shot” for something I knew nothing about. My mother said to me “Better you should cry than I should cry”. I got the vaccine although I was not happy about it.

One of the issues with growing up in New York in the 1950s is we had three professional baseball teams, the Brooklyn Dodgers, New York Yankees, and New York Giants. I was obsessed with baseball and later realized it was my introduction to statistics, a big help in my later career.

Two major factors contributed to my interest in science. In 1957, the launch of Sputnik showed me the power of science. And the second factor was my mother. She had wanted to become a physician and had been admitted to medical school but did not go because of financial concerns during the depression years and available money needed to be used to assure her younger brother could get an undergraduate degree. She passed her interest in medicine on to me.

I went to the Bronx High School of Science and was stimulated by my high school chemistry teacher making me want to be involved in a career associated with chemistry. Following graduation, I attended the City College of New York (CCNY), which I loved. I was a “pre-med” major with a focus on chemistry. I received a New York State Regents Scholarship for medical school and decided to stay in New York, attending the Albert Einstein College of Medicine. Although only about a mile from where I grew up, I finally moved out of my house. I had thought I would go into internal medicine but happened to be assigned to Montefiore Hospital for my pediatrics clerkship and was fortunate to have the Chairman of Pediatrics, Laurence Finberg, as my attending. He was amazing. He seemed to know everything about everything although his special expertise was in fluid and electrolytes, compatible with my interest in chemistry. It was his recommendations in support of me that changed my life because they got me the internship I wanted and into the Epidemic Intelligence Service (EIS) at the Centers for Disease Control and Prevention (CDC).

In 1965, while a Boy Scout, I went on a trip with eight other scouts around the country and fell in love with San Francisco. Thus, when it came to pediatric internships, my first choice was the University of California, San Francisco. I thought I would live my whole life there and become a pediatric nephrologist, in line with my interest in chemistry. But in the early 1970s, there was a service obligation. While in medical school, I contacted my cousin, Harry Rubin, the “doctor” in the family for advice. He told me he had been an EIS Officer at the CDC in the class of 1956 and said he got to travel a lot. Having lived my whole life in The Bronx up to that point, I was really intrigued by the promise of travel so I applied to the EIS and was admitted. I decided to enter the EIS in the class of 1974. I wanted to stay west so my top three choices for an assignment were Los Angeles (I could not take Berkeley because of EIS rules at the time), followed by Denver and Phoenix. I felt I needed to choose at least one Atlanta assignment and after looking through those available, I decided on the Immunization slot, based at the CDC, since immunization was such an important part of pediatrics. I was really disappointed when I got my fourth choice, immunization, but I thought it would be only 2 years and that I would go back to San Francisco afterward, finish my pediatrics training and then train in nephrology.

When I got to CDC, given my interest in travel, I volunteered for every international opportunity (did not get the first few). And with CDC’s efforts to play a major role in the smallpox eradication program, an opportunity became available to work in India. In December 1974, I went to India and was assigned to the smallpox eradication program in Uttar Pradesh (UP), India’s largest state in population, located in north-central India and bordering on Nepal. That assignment changed my career and my life. I saw a disease with about a 30% case-fatality rate disappear before my eyes because of a vaccine. In addition, I saw how epidemiology was being used to terminate transmission. The original strategy for smallpox eradication was mass vaccination. But careful analysis showed surveillance and containment or “ring vaccination” in which cases were identified and isolated so they could not transmit further, primary contacts were enumerated and vaccinated, and contacts of the contacts were also identified and vaccinated, was more effective. We got the names of all these contacts and kept going back to them until they accepted vaccination, my first experience dealing with vaccine hesitancy. During my time in UP, we terminated transmission. The last case of smallpox in UP was Shanti, the 7-month-old daughter of Pyari Lal, who died in Aligarh in March 1975. She was a tragic case because she might have been protected had her brother’s earlier case been reported since smallpox vaccination can sometimes
prevent disease when administered after exposure. But her father was hesitant and did not report the case to our worker.

My mentors in smallpox were keen on getting rid of measles. They had worked in West Africa at the beginning of the smallpox eradication program and saw the devastation of measles, a disease with more adverse health outcomes than smallpox in that setting. They wanted me to try the surveillance and containment approach to terminating measles transmission in the United States. The CDC was in charge of a major grant program (the 317 grant program) to each of the states in which CDC could require states to do certain things and we required them to focus on measles outbreak control. In retrospect, this made little sense. Smallpox was considerably less contagious than measles with a basic reproduction number (Ro) of 5–7 compared to measles with a Ro of 12–18. Further, smallpox usually did not become contagious until the patient was pretty sick. Whereas with measles, contagiousness usually begins with the prodrome during which the patient is not very sick and can be mobile. With smallpox, transmission could be predicted easily. With measles, prediction was very difficult. But frustration in the field with the surveillance and containment approach had other benefits. It motivated innovation and specifically led the Director for Acute Communicable Diseases in Los Angeles County to exclude students who were not vaccinated from school to try to control an ongoing outbreak in the county. She excluded approximately 50,000 of 1.4 million students from school and this became the standard way to control outbreaks. And soon people realized we should not be in the business of controlling outbreaks but preventing them and this played a major role in the first Presidential Initiative on Immunization in the late 1970s in leading to the enactment and this enforcement of comprehensive school laws covering all children from kindergarten to 12th grade requiring immunization for attendance. Data collected showed states vigorously enforcing school laws had much lower incidence rates of measles than states with laxer enforcement and this promoted states to take more aggressive efforts to implement and enforce school laws.

In the early 1980s, as we investigated measles outbreaks, we became concerned about vaccine failures and whether vaccine effectiveness in the field was lower than that found in the clinical trials. This required determining the level of measles vaccine effectiveness (VE) in observational studies and led to a review of the various methods available and their strengths and weaknesses. Some of my earliest work dealt with a review of various methods to estimate VE including the development of the “screening” method, which used existing data from surveys or other sources to estimate the proportions of the population which were vaccinated and vaccination status of the cases to calculate attack rates in vaccinees and non-vaccinees to estimate VE. We constructed a graph to show the expected proportions of vaccine failure given a particular vaccination coverage and vaccination status of cases. For example, if an outbreak occurs in a population with 90% coverage and the VE is 90%, then approximately 50% of cases would be expected to have a history of vaccination. This was very helpful in explaining proportions of cases which were vaccine failures.

As time went on, we began to notice there were different patterns of measles outbreaks. We developed a classification system for cases based on my experience with baseball as a child. In baseball, an earned run is the pitcher’s fault. In essence, it was a failure of the strategy which counts on the pitcher to assure every hitter either strikes out or hits a ball that can easily be converted to an out. In contrast, an unearned run was not the pitcher’s fault because someone else on the field had made errors which allowed the run to happen. Thus, this is a strategy implementation failure. The player who should have been out was safe because the fielder failed to implement appropriately. When measles outbreaks primarily involved preschool-aged children, most of the cases were in children who should have been vaccinated but were not. Based on my experience in baseball as a child, we called this programmatic failures (i.e., strategy implementation failures or “preventable cases” – in other words “unearned runs”). In contrast, when outbreaks primarily involved school-aged children, the greatest proportion of cases was in persons who had had the recommended one dose of vaccine but still got measles. These were “strategy failures” since only one dose was recommended at the time and we called them “non-preventable” (in other words “earned runs”). Theoretically, all cases of measles are preventable, some directly by vaccination, and others indirectly if they are not exposed to the virus because of high levels of immunity in the population (i.e., herd immunity). But the classification system was helpful. It led to the recommendation of a second dose of measles vaccine to reduce most of the “non-preventable cases” and a second Presidential Immunization Initiative in the early 1990s, called the Childhood Immunization Initiative (CII), to address most of the “preventable” cases by removing cost as a barrier to vaccination and more.

In 2004, I left CDC to go to Emory University, as a Professor of Internal Medicine in the Division of Infectious Diseases as
well as Associate Director of the Emory Vaccine Centre. During this period, I focused my work on a variety of vaccine-related issues including evaluation of the test-negative case-control study design for measuring influenza vaccine VE, now the standard method used in the United States. A goal of the test-negative design was to try and correct for biases potentially introduced by differences in healthcare-seeking behavior between vaccinees and non-vaccinees since both cases and controls included persons who sought medical care for a respiratory illness and were tested for influenza. The cases were influenza-positive and the controls were influenza negative. During my initial time at Emory University, I also worked on issues of vaccination implementation particularly with regard to factors associated with uptake of influenza vaccine.

In 2008, I left Emory University to go to the Bill & Melinda Gates Foundation (BMGF) as Deputy Director for Immunization Programs, with a special focus on polio eradication. Among the grants I managed were grants to address vaccine hesitancy globally, support of the global measles initiative, as well as a number of grants to support the Global Polio Eradication Initiative. The polio grants included major funding to the World Health Organization (WHO), the Rotary Foundation, and UNICEF to work to terminate polio transmission. During my 3 years at the Foundation, we laid the groundwork for establishing critical groups to independently evaluate progress in achieving polio eradication. The Independent Monitoring Board (IMB), which initially met the year after I left the foundation provides critical input into current and future strategies for polio eradication.

In 2011, I returned to Emory University, working particularly on influenza, vaccine hesitancy and vaccine policy issues I served as Chairman of the National Vaccine Advisory Committee (NVAC) from 2012 to 2016 and presided over multiple recommendations including a report on Global Immunization which tried to make the case that US support of global immunization had both humanitarian benefits to the countries receiving assistance as well as helping our own domestic health security by reducing the threat of importations of vaccine-preventable diseases. Overall, during my period as Chair, NVAC published 11 reports including recommendations related to Standards for Adult Immunization Practices, Assessing the State of Vaccine Confidence, A call for greater consideration of vaccines in combatting antibiotic-resistant bacteria, and more (https://www.hhs.gov/vaccines/nvac/reports-and-recommendations/index.html, accessed 10-13-19). During my period at Emory University, I have been the Principal Investigator on an NIH contract entitled the Emory-UGA Centre of Excellence for Influenza Research and Surveillance (Emory-UGA CEIRs). This contract covers work on influenza pathogenesis, immunology, animal surveillance and more. I led an effort for WHO to do a midterm review of the Global Measles-Rubella Strategic Plan (2012–2020) and became a member of the WHO Strategic Advisory Group of Experts on Immunization (SAGE) Working Group on Measles and Rubella. I am also a member of the SAGE Polio Working Group.

Perhaps one of my greatest honors was to be asked to be a co-editor of the textbook “Vaccines”, the standard textbook in the field of vaccinology. I have been a co-editor for the last 5 editions, the last named “Plotkin’s Vaccines” published in 2018.

And I will always be thankful to my wife and children, who continuously and vigorously supported my career.

In summary, we have highly safe and effective vaccines. But if they are not administered to the persons for whom they are recommended, there is no impact. In essence, vaccines which remain in the vial are 0% effective, no matter what the results of the clinical trials showed. Persons for whom vaccines are recommended need to receive them if there is to be a benefit to the individual as well as society. This requires implementation of science research to determine why persons are not being vaccinated and taking steps to overcome the barriers. For example, in the US, a major problem during the late 1980s and early 1990s was barriers to access including financial barriers, requiring steps to remove them. Other problems especially currently involve vaccines hesitancy and overcoming it by building confidence. In conclusion, vaccines do not save lives. Vaccinations save lives.

Notes on contributor

About Walter Orenstein: Dr. Orenstein is a Professor of Medicine, Epidemiology, Global Health, and Pediatrics at Emory University. From 2008 through 2011, Dr. Orenstein was Deputy Director for Immunization Programs at the Bill & Melinda Gates Foundation. His primary focus at the foundation had been on polio eradication, measles control, and improving routine immunization programs. Prior to 2004, Dr. Orenstein worked for 26 years in the Immunization Program at the Centers for Disease Control and Prevention. In 1988-2004, he was the Director of the United States Immunization Program. He is a former Assistant Surgeon General of the United States Public Health Service.

Dr. Orenstein successfully developed, promoted, facilitated and expanded new vaccination strategies to enhance disease prevention. Walter Orenstein has authored and co-authored numerous books, journals and reviews. He co-edited Plotkin’s Vaccines, 7th edition in 2018 – the leading textbook in the field. He is a past Chair of the WHO’s Poliomyelitis Technical Consultative Group and served as the Chair of the National Vaccine Advisory Committee (NVAC) from 2012 to 2016. He is also currently a member of the WHO’s Strategic Advisory Group of Experts (SAGE) on Immunization Polio as well as Measles and Rubella Working Groups. Between July 1, 2016 and June 30, 2018, Dr. Orenstein was the President of the National Foundation for Infectious Diseases (NFID).

Dr. Orenstein’s research focus has been on assessment of vaccine effectiveness in observational studies, methods to overcome vaccine hesitancy, ways to enhance uptake of recommended vaccines, and ways to facilitate polio eradication and sustain that eradication. In addition, Dr. Orenstein is the Principal Investigator for an NIH funded Center of Excellence for Influenza Research and Surveillance, with a focus on better understanding pathogenesis, immune responses to vaccines and infection, and viral surveillance in animal populations.

References


