

Fostering Further Successes in Vaccinology



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Vaccination—preparing or harnessing the power of the human immune system to prevent infectious diseases—is one of the most impactful developments in the history of public health.¹ In more than two centuries of clinical use, vaccines have been responsible for preserving the health and preventing the deaths of millions of children and adults annually.² There are several examples in which the widespread and routine use of vaccines has greatly reduced or eliminated infectious diseases from selected geographic regions or hemispheres of the globe. Vaccines enabled the eradication of naturally occurring smallpox from the world—a remarkable achievement with neither precedent nor peer in the realm of medicine.³ Yet despite the proven track record of vaccine safety and effectiveness, there remain several significant barriers that impede their further development, acceptance, and broader implementation.

There is clear evidence that vaccines prevent illness, hospitalization, and death and that their use promotes economic savings through medical and social costs avoided.^{4,5} However, their favorable impact has made vaccine-preventable diseases less common and thus, less visible. The commonly applied outcome metrics used when making the case for investments in vaccines become far less important to policy-makers, the public, and to parents when the preventive measures work and over time, the benefits provided by vaccines become less visible and compelling.⁶ For many in the developed world, including physicians, the vaccine-preventable, classic scourges of childhood such as polio, pertussis, diphtheria, measles, and mumps primarily represent historical footnotes.⁷ But before the advent of safe and effective vaccines, these infectious diseases caused significant morbidity, mortality, and lingering fear in communities.⁸

As a society, we now tend to take for granted the improvements in public and individual health engendered by the successful development and deployment of vaccines. However, outbreaks of vaccine-preventable diseases, which are becoming more frequent in the developed world, serve as frightening and costly reminders of the value and benefits of vaccines. Multiple examples of such outbreaks have occurred over the past decade. Measles, a highly transmissible viral disease that was once considered to have been eliminated in many countries in the developed world as a result of vaccination, has resurged in epidemic form in multiple European countries and outbreaks in the U.S.^{9–11} The incidence of mumps had fallen by more than 99% in the U.S. since the introduction of an effective vaccine in 1967, but recent outbreaks of this disease have occurred among college students,¹² Orthodox Jewish communities,¹³ and others.¹⁴ Annual incidence rates of pertussis, a highly morbid, acute infectious respiratory disease, have risen by more than six-fold over the past two decades.¹⁵ The etiologies of such outbreaks are varied, ranging from biological—reduced efficacy and waning vaccine immunity¹⁶—to sociological—vaccine refusal and other reasons for suboptimal vaccination uptake.¹⁷

In the developing world, where many vaccine-preventable infectious diseases are endemic and outbreaks are more frequent and of broader scope than in the developed world, several challenges and barriers to vaccines or widespread vaccination persist. Some of these are economic (e.g. vaccine costs and financing), but many are related to the local social, cultural, political, immunologic and microbiologic issues in these environments.¹⁸ The ongoing effort to control epidemic meningococcal meningitis in sub-Saharan Africa necessitated the formulation and manufacture of an African-specific, group A meningococcal conjugate vaccine that met regional scientific and economic imperatives.¹⁹ The campaign to eradicate polio, now into its second quarter-century, remains unfinished despite vaccinating over 2.5 billion children,²⁰ with the final steps in the process having to overcome significant cultural, political, and ideological challenges. Additionally, several of the most important infectious diseases of the developing world, such as malaria and HIV-1, continue to scientifically elude an effective vaccine solution.

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This special issue represents a unique collaboration between two scientific journals: the *American Journal of Preventive Medicine* and *Vaccine*. Our primary aim is to provide an educational resource regarding vaccine safety, efficacy, and implementation to inform health care professionals and policy makers and to promote the optimal use of some of medicine's most highly valued interventions. Although the topics cover a broad spectrum of important issues in vaccine science, the overarching theme revolves around identifying barriers to vaccination and providing insights that will help foster continued and further success.

Several papers address scientific and biological barriers to vaccination. HIV-1, malaria, and dengue are worldwide infections that affect hundreds of millions of people annually. They are each complicated by distinct biological issues that have hindered the development of effective vaccines. In their papers on the outlook for globally effective vaccines against these three infections: HIV-1 by Excler and colleagues,²¹ malaria by Hoffman and colleagues,²² and dengue by Thomas and Rothman,²³ the authors examine how pathogen biology has guided the direction of basic, vaccine research efforts and how these efforts have informed clinical trials. In each case, the scientific advances appear to be leading to critical vaccine breakthroughs.

Influenza represents another example of a scientific barrier to vaccination addressed in this volume. Although a seasonal vaccine approach to influenza has existed for 70 years, a biological property of the virus—antigenic variation—has impeded the development of a universally effective, durable product.²⁴ Treanor reviews the current status and provides an assessment of future vaccine platforms for influenza that address this difficult issue.²⁵ As Harrison's article on the development and implementation of effective vaccines targeting group B meningococcal disease illustrates, it is possible to successfully overcome certain biological challenges to vaccination.²⁶ Vaccine prevention was stymied for decades as group B meningococcus exhibits molecular mimicry with human tissue antigens and subsequently induces immunologic self-tolerance.²⁷ The paper highlights how the application of several novel scientific processes addressed this challenge.

Safety concerns represent another potential set of challenges to the use of vaccines or the universal adoption of vaccine recommendations. Chen and colleagues provide a broad overview of the issues and all of the ramifications by providing a global view of safety from a vaccine lifecycle perspective.²⁸ Safety experience accrued from the use of licensed vaccines is viewed through the lens of rotavirus vaccines by Parashar and colleagues.²⁹ The authors assess the impact of post-licensure safety and efficacy data on vaccine policy in this arena. Finally, Pilishvili and Bennett describe the considerations that

informed recent policy recommendations regarding the strategic implementation of new, effective pneumococcal vaccines among distinct age groups.³⁰

Other papers examine the promise and the challenges related to the optimal utilization of safe and effective vaccines. Hinman and McKinlay call attention to the value and roles that vaccines and vaccination recommendations can play in reducing health inequities and fostering access to health care.³¹ Their paper, which reviews data from surveys conducted in developing countries from 2005 to 2011 that show significant inequities in immunization coverage, describes several initiatives currently underway directed at increasing childhood immunizations and reducing health inequities. Shrivastwa and colleagues provide a closer look at India, a country with one of the lowest immunization rates in the world despite a longstanding Universal Immunization Program that provides free vaccines.³² The authors use immunization coverage data to identify the factors that affect whether children receive recommended vaccines. Their aim is to develop interventions for reducing disparities among children in different demographic and cultural groups.

Vaccine hesitancy, or a reluctance to accept recommended vaccines, is receiving more attention worldwide, especially in the U.S. where efforts are underway to foster greater vaccine acceptance. Salmon and colleagues review the factors that contribute to vaccine hesitancy, the potential relationship between hesitancy and vaccine coverage among children, and possible strategies for addressing hesitancy. Although their focus is on the U.S., much of what is discussed has relevance for immunization programs across the globe.

Four articles build on the theme of overcoming barriers, including vaccine hesitancy, and provide insights that can foster vaccine acceptance and vaccination program success by examining selected vaccine experiences in the U.S., including efforts directed at specific sub-populations. Walton and colleagues examine the process by which vaccination recommendations have been made and implemented in an effort to highlight "lessons learned" that can inform future decisions and other countries.³³

In the U.S., the Advisory Committee on Immunization Practices (ACIP) uses a rigorous process to make recommendations to determine if and how licensed vaccines should be used. Their scope encompasses childhood, adolescent, and adult vaccines; the articles by Weiner et al.,³⁴ Dempsey and Zimet,³⁵ and Lu and colleagues³⁶ provide insights into these respective domains. Weiner and colleagues examine the vaccine-related knowledge, understanding, and information-seeking habits of first-time mothers who are in their second trimester of

pregnancy. Often, vaccine-related beliefs and behaviors are shaped early; this study highlights both the challenges and opportunities for fostering childhood vaccination acceptance. Dempsey and Zimet take a similar look at the challenges involved in fostering adolescent vaccination. The authors identify and describe approaches that have either had success or hold promise regarding the four vaccines currently recommended for routine administration to all adolescents in the U.S. Finally, Lu et al. assess adult vaccination by race/ethnicity in the U.S. using the 2012 National Health Interview Survey. They find that adult vaccination coverage remains suboptimal, particularly among racial and ethnic minority groups. They also suggest that progress can be made on both fronts—improving coverage and eliminating disparities—through greater implementation of evidence-based interventions.

We believe the articles in this special issue not only provide readers with a wealth of information and insights into the world of vaccines but also provide a strong foundation to inform continued progress. In spite of the remarkable success of immunizations at preventing disease, it will take further efforts by researchers and public health professionals throughout the world to realize the full benefits of available vaccines and to extend their promise beyond what is possible today. Vaccines are essential to making progress in overcoming the global burden of infectious diseases. As this collection of articles illustrates, the journey will not be easy—with new challenges likely to emerge and existing ones likely to persist—but the rewards in terms of health and health equity are great.

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