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From the Guest Editors

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We are living in an interesting and challenging time when it comes to immunizations. One of the greatest triumphs in this current pandemic has been the development of very effective and safe vaccines for COVID-19. Amazingly, they were ready to go into arms 11 months after the genome of the virus was first sequenced. These vaccines will take us out of the pandemic, and presumably into the endemic phase of COVID-19, for which we are likely to need vaccines for the foreseeable future. But beyond COVID, other great things have been happening in the field of immunizations. Advances in immunology, molecular biology, and genetics have resulted in groundbreaking developments in vaccinology. In addition, the advent of population-based post licensure reporting of potential adverse effects has contributed greatly to the current safety of vaccines.

The History of Immunization Programs

The goals of immunization in the human population include prevention of infection, elimination of a disease, and ultimately eradication of the pathogen. To date, four viral pathogens have been eradicated from the world, including smallpox, polio virus type 2, poliovirus type 3, and the veterinary pathogen rinderpest. Measles was declared eliminated in the United States in the year 2000 (meaning no endemic transmission for the preceding 12 months). The U.S. almost lost that status in 2019, owing to significant endemic transmission of measles related to lower rates of immunization in certain populations. Most vaccine preventable diseases are at historic lows, compared with rates prior to the availability of vaccines.

We like to refer to an article that was published in the MMWR several years ago which we call "731,700 Reasons to Celebrate Vaccines." This study looked at rates of 13 vaccine preventable diseases in the modern era in a cohort of children born in the United States from 1994 to 2013 compared with rates prior to the availability of vaccines. Over 322 million illnesses, 21 million hospitalizations, and 731,700 deaths were prevented as a result of vaccines (figure 1).[1]

Figure 1. Data on Estimated Illnesses, Hospitalizations, and Deaths Prevented by Routine Childhood Immunization, 1994-2013[1]

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TABLE. Estimated number of illnesses, hospitalizations, and deaths prevented by routine childhood immunization for selected vaccine-preventable diseases among children born during the Vaccines for Children era — United States, 1994–2013

Vaccine-preventable disease*	Cases prevented (in thousands)		
	Illnesses	Hospitalizations	Deaths
Diphtheria	5,073	5,073	507.3
Tetanus	3	3	0.5
Pertussis	54,406	2,697	20.3
Haemophilus influenzae type B	361	334	13.7
Polio	1,244	530	14.8
Measles	70,748	8,877	57.3
Mumps	42,704	1,361	0.2
Rubella	36,540	134	0.3
Congenital rubella syndrome	12	17	1.3
Hepatitis B	4,007	623	59.7
Varicella	68,445	176	1.2
Pneumococcus-related diseases†	26,578	903	55.0
Rotavirus	11,968	327	0.1
Total	**322,089**	**21,055**	**731.7**

* Vaccines were considered as preventing disease for birth cohorts born in all years during 1994–2013 except for the following, which were only in use for part of the 20-year period: varicella, 1996–2013; 7-valent and 13-valent pneumococcal conjugate vaccines, 2001–2013; and rotavirus, 2007–2013.

† Includes invasive pneumococcal disease, otitis media, and pneumonia.

As exciting and important as the results of US childhood immunization have been, developments in the world of adult immunization have been equally impressive. When one of us (S.E.) entered medical school, the only routine vaccine for adults was the flu shot; the first pneumococcal vaccine came about when he was a junior medical student. We now have highly effective, multivalent pneumococcal conjugate vaccines that have made a huge difference in invasive pneumococcal infection in adults, as well as in children. The US Centers for Disease Control and Prevention (CDC) is emphasizing the importance of hepatitis B immunization of adults, and we now have a highly effective adjuvanted vaccine against hepatitis B. Herpes zoster (shingles) can be a terrible condition; we now have a very effective recombinant vaccine that can prevent 90% of cases. Human papilloma virus (HPV) causes over 40,000 cases of cancer in the United States each year. The current vaccine has the potential to markedly reduce those numbers, and we are already seeing real-world effects of the virus on HPV-associated conditions. There are other vaccines that are routinely given to adults, or are recommended for adults with certain risk factors. The current 2022 CDC recommended vaccine schedule can be found within this issue, and online.

The Future of Immunizations

There are many challenges and opportunities in the developing world regarding immunization, and readers should remember that vaccine preventable diseases are at most 18 hours away by plane from any part of the world. As we mention elsewhere in this issue, there are reasonably effective cholera vaccines (orally administered, one of them FDA-approved). In 2020, there were 241 million cases of malaria worldwide, resulting in 627,000 deaths. But this year, the introduction of an effective malaria vaccine ("RTS,S" more easily remembered by the trade name Mosquirix) has the potential to truly transform those numbers. Dengue, another mosquito-borne disease (albeit via a different mosquito--the Aedes species, which can also transmit Zika

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and yellow fever), affects over 100 countries worldwide. Affecting greater than five million cases globally, there is an effective vaccine (the FDA-approved Dengvaxia).

HIV remains one of the most elusive viruses for which we are still working to develop a vaccine. Given the worldwide morbidity and mortality from AIDS (33 million deaths since the start of the epidemic), there has been predictable interest in the topic, but relatively little progress until recently. Utilizing mRNA technology, a promising HIV vaccine is being trialed by Moderna this year (the name *Moderna* is itself a mashup of the terms 'modified' and 'RNA').

> It is worth mentioning that, while "mRNA vaccines" entered our popular lexicon recently via COVID-19 vaccination, the technology has been around for decades. In 1987, Dr. Robert Malone, then a graduate student at the Salk Institute in California, started experimenting with mRNA for vaccines (and also started a convoluted chain of disputed ownership and intellectual property rights). What remained clear was that mRNA was seen as sufficiently difficult to work with. Slow advances were catalyzed by funding in 2015 by the US Defense Advance Research Projects Agency (DARPA), which provided seed funding for mRNA vaccines and therapeutics. Moderna was one the companies to be built by the funding; when in 2020 the COVID-19 genome became available, they collaborated with the US National Institute of Allergy and Infectious Diseases (NIAID, the agency led by Dr. Anthony Fauci), to rapidly conduct clinical trials. BioNTech, another company developing mRNA technology, partnered with Pfizer to achieve a similarly rapid outcome. Both companies, along with many others including Janssen and AstraZeneca, ultimately developed COVID-19 vaccines.

Vaccines and Delaware

In resource-rich countries like the U.S., comprehensive immunization programs provide consistently high levels of vaccine coverage, and are incredibly effective public health measures, dramatically reducing the incidence of all vaccine preventable diseases. The State of Delaware, in general, compares favorably with other states in immunization rates. We must continue to have high immunization rates or suffer the possibility of resurgence of vaccine preventable diseases. In this regard, vaccine hesitancy (the subject of several articles in this issue of Delaware Journal of Public Health) presents major challenges.

Figure 2. Logo of the Immunization Coalition of Delaware

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Dr. John O'Neill, author of one of the articles in this issue, and Dr. Eppes co-chair the Immunization Coalition of Delaware (https://immunizedelaware.org, figure 2). Most of the Coalition's successes, however, are the result of work done by Dr. Kate Smith who, among her other roles, is Copy Editor for the Journal. The ICD was formed in 2006 in conjunction with the Delaware Division of Public Health, and is a program of the Delaware Academy of Medicine/Delaware Public Health Association. The ICD consists of a diverse group of passionate, energetic, and committed partners working together to advocate for, educate about, and provide access to vaccination, and to ensure that no one in Delaware suffers from vaccine preventable illnesses.

References

1. Whitney, C. G., Zhou, F., Singleton, J., & Schuchat, A., & the Centers for Disease Control and Prevention (CDC). (2014, April 25). Benefits from immunization during the vaccines for children program era - United States, 1994-2013. *MMWR. Morbidity and Mortality Weekly Report*, *63*(16), 352–355. PubMed