Vaccines: Can Transparency Increase Confidence and Reduce Hesitancy?

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KEY WORDS

vaccine safety, vaccine confidence

ABBREVIATIONS

Hib—*Haemophilus influenzae* type b

IOM—Institute of Medicine

MMR—measles, mumps, and rubella

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Vaccines are one of the most successful public health achievements of the 20th century^{1–3} and have contributed to improved health and longevity for millions of people in the United States.^{2–4} Between 1900 and 2000 the average life expectancy in the United States increased by >30 years, from 43.7 to 76.8 years, and infant mortality through 12 months of age decreased from 100 per 1000 population to <7 per 1000 population.^{2,5} The decrease or elimination of vaccine-preventable infections played a critical role in these population outcomes that have positively influenced the health, growth, and economy of our nation.

An evaluation of the US vaccine program from 1900 to 1998 demonstrated reduction or elimination of many infectious diseases that had resulted in substantial childhood morbidity and mortality, including smallpox, diphtheria, pertussis, tetanus, polio, measles, mumps, rubella, and *Haemophilus influenzae* type b (Hib).² Newer vaccines, including those that target pneumococci, human papilloma virus, influenza, rotavirus, and varicella, are also reducing morbidity and mortality. Modeling of vaccine impact demonstrates that routine childhood immunizations in the 2009 US birth cohort would prevent ~42 000 deaths and 20 million cases of disease and save \$13.5 billion in direct health care costs and \$68.8 billion in societal costs.³ The Vaccines for Children program, operating since 1994 to provide vaccines at no cost to low-income children, has eliminated racial and ethnic disparities in immunization coverage, ensuring that all US children have an opportunity to enjoy the benefits of vaccines.⁶

Despite the public health triumphs of vaccines or perhaps because the triumphs have created an environment where the ravages of vaccine-preventable disease have been forgotten, confidence in vaccines has decreased in the 21st century, and the number of parents who hesitate to immunize their children is increasing.⁷ Rates of nonmedical personal exemptions for vaccines are also increasing and have been associated with outbreaks of vaccine-preventable infections, including pertussis and measles.^{8,9}

Parental concerns about vaccine safety have been recognized as an important factor that may result in delaying or forgoing vaccines.^{10,11} However, the US commitment to vaccine safety is multilayered and includes rigorous prelicensure studies reviewed by the Food and Drug Administration and both active and passive surveillance systems through the Centers for Disease Control and Prevention Vaccine Safety Datalink and the Centers for Disease Control and Prevention and Food and Drug Administration Vaccine Adverse Events Reporting System. The systematic evaluation of published studies by Maglione et al¹² adds another layer of transparency to evaluation of vaccine safety in the United States. The evidence report, commissioned by the Agency for Health Research and Quality, describes the adverse events associated

with vaccines in routine use in the United States for children ≤ 6 years old. The data presented confirm and update the 2011 Institute of Medicine (IOM) report⁵ and expand the scope of the report to include Hib, hepatitis A, pneumococcal conjugate 13, rotavirus, and inactivated polio vaccines.

In this well-done analysis, the authors present high-quality evidence that there is no association of childhood leukemia with numerous vaccines and no association of autism with the measles, mumps, and rubella (MMR) vaccine. The authors present moderate-quality evidence of no association of the diphtheria, tetanus, and acellular pertussis vaccine with diabetes mellitus, no association of the hepatitis B vaccine with multiple sclerosis, and no association of serious adverse events with the Hib vaccine.

The authors did report adverse events associated with vaccines, including high-quality evidence that the MMR vaccine is associated with febrile seizures and the varicella vaccine is associated with complications in immune-deficient people. There was moderate-quality evidence for purpura associated with the hepatitis A and MMR vaccines, febrile seizures with the pneumococcal conjugate 13 vaccine, and intussusception with rotavirus vaccines.

The adverse events identified by the authors in their evidence review were not unexpected. Clinicians who immunize children regularly may have encountered these adverse events in their practices, particularly seizures associated with fever. Fortunately, the adverse events identified by the authors were rare and in most cases would be expected to resolve completely after the acute event. This contrasts starkly with the natural infections that vaccines are designed to prevent, which may reduce the quality of life through permanent morbidities, such as blindness, deafness, developmental delay, epilepsy, or paralysis and may also result in death.

The findings of the IOM report and of the Maglione et al study should be reassuring to parents of young children and to the clinicians who care for them. However, a recent report evaluating the effectiveness of messages designed to reduce parental misperceptions and increase vaccination rates, including messages about vaccine safety, demonstrated that these messages were ineffective and in some groups of parents may even reduce the intention to vaccinate.¹³ These data suggest that alternative strategies to bolster parental confidence in vaccine safety are needed.

If parents are not convinced by safety data, perhaps these data can be used to

increase clinicians' confidence in the safety of the US vaccine schedule. Data indicate that recent medical graduates are more skeptical of vaccine efficacy than older graduates,¹⁴ and in 1 state more than one-half of medical providers were willing to consider untested immunization schedules for at least some vaccines.¹⁵

The relationship between parents of young children and their medical providers is powerful. Parents trust their child's doctor over government officials, family members, or celebrities as the best source of information on vaccine safety.^{16,17} Furthermore, there is concordance between the beliefs of parents and the beliefs of their child's health provider about vaccine safety.¹⁸ Importantly, data also demonstrate that for parents who are hesitant to immunize their children but who ultimately do so, it is the physician's recommendation that is most often cited as the reason they chose to vaccinate. Clinicians can examine the nonbiased data presented in the IOM report and the report by Maglione et al to increase their own confidence in vaccine safety and their advocacy for vaccines. Ideally, provider confidence in vaccine safety will increase the confidence of the families they serve and increase vaccination rates for children, safeguarding the health of the nation.

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THE FOUNTAIN OF YOUTH: For most of recorded time, humans have searched for a potion that would restore youth to anyone who drank or bathed in it. Herodotus wrote of a fountain with such miraculous waters in the 5th century BC. The letters of the medieval Prester John suggested that such a Fountain of Youth was in current day Ethiopia. In the early 16th century, Ponce de Leon, the first governor of Puerto Rico, was searching for the Fountain of Youth when he began exploring what is now known as Florida. More recently, however, scientists may have actually discovered critical molecules in the blood that can restore aging tissue.

As reported in The New York Times (Science: May 4, 2014), researchers have known for several years that blood from young mice continuously infused into old mice reversed some aspects of aging. For example, the cartilage did not disintegrate or – more impressively – more and new neural connections were made. Initially thought to be due to stem cells, studies suggested that older mice had a reasonable complement of stem cells; they just weren't getting the correct signals. Screening their blood led to the discovery of a protein called GDF11 that was abundant in young mice but uncommon in older mice. GDF11 injected into old mice rejuvenated both hearts and muscles, making the mice stronger and fitter. GDF11 injected into brains of old mice stimulated the growth of blood vessels and neurons, but not as much as plasma from young mice – suggesting that additional factors may be at play.

Undoubtedly, there will be keen interest in learning if similar molecules exist in humans and whether they could affect the aging process and diseases such as Alzheimer's. While the data are exciting and promising, explorers have been searching for the Fountain of Youth for some time. And, as we know from Greek myths, there are always major problems with being granted everlasting life or youth. We will have to learn if infusion of GDF11 or other such molecules increase the risk of other conditions such as cancer. Stay tuned.

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