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An Informed Approach to Vaccine Hesitancy and Uptake in Children

Jonathan M. Miller, MD, FAAP [1] and Ricki S. Carroll, MD, MBE [2]

1. Chief, Primary Care; Medical Director, Value Based Care, Nemours Children's Health; Clinical Associate Professor, Pediatrics; Sidney Kimmel Medical College, Thomas Jefferson University

2. Attending Physician, Divisions of Orthogenetics & Palliative Medicine, Nemours Children's Health; Clinical Associate Professor, Pediatrics, Sidney Kimmel Medical College, Thomas Jefferson University

Abstract

The tremendous success of vaccination programs worldwide over the past two centuries has produced a paradoxical effect whereby a lack of exposure to the devastating consequences of vaccine-preventable diseases has created an environment in which fear of the side effects of vaccines can overshadow concerns about the impact of the diseases they are meant to prevent. As vaccine hesitancy grew over the past twenty years, states passed legislation, such as non-medical exemptions from vaccination, that have cultivated pockets of poor vaccine uptake allowing for the return of vaccine-preventable diseases such as measles and pertussis. The COVID-19 pandemic has further intensified mistrust of vaccines, impacting both the reasons for vaccine hesitancy and the attributes of vaccine hesitant parents. Because unimmunized children are at increased risk for vaccine-preventable diseases and associated cancers, as well as reduced access to adequate healthcare, they are a particularly vulnerable population warranting special protections and support. A comprehensive approach to combat vaccine hesitancy and promote uptake should include a focus on evidence-based initiatives at the legislative, practice, and provider levels. These strategies can substantively inform health policy, from upstream legislation strengthening school mandates and eliminating non-medical exemptions to downstream policies that impact provider conversations about immunization.

Introduction

The World Health Organization (WHO) considers immunization to be "one of modern medicine's greatest success stories," and the Centers for Disease Control and Prevention (CDC) listed vaccination at the top of the list of the "Ten Great Public Health Achievements" of the 20th century.[1,2] Despite the estimated 2-3 million deaths prevented each year by immunizations, vaccine hesitancy has been growing over the past 25 years, leading to the WHO naming vaccine hesitancy as one of "ten threats to global health" in 2019.[3] The COVID-19 pandemic has intensified the backlash against vaccination programs and highlighted disparities in vaccination access and uptake.

Fundamental to a fully informed immunization debate is an understanding of the efficacy and significance of vaccines. Global vaccination programs are responsible for the eradication of smallpox, the loss of endemic status for measles and polio in many countries around the world, including the eradication of wild-type polio from the African continent, and the saving of countless lives from vaccine-preventable diseases.[4]

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The majority of immunizations recommended for routine use in children in the United States have efficacy of over 90%, with some, such as polio and measles, approaching 99%.[5] The side effect profiles of these immunizations are quite favorable, typically encompassing local reactions or transient systemic symptoms such as fever. Fortunately, the vaccinations routinely recommended for children have no serious, long-term side effects. The serious adverse effects of these vaccines, such as anaphylaxis or febrile seizures, are rare and not associated with long-term sequelae when treated appropriately. Studies have repeatedly failed to demonstrate a link between immunizations and developmental changes such as autism, but that has not prevented the anti-vaccination movement from continuing to gain momentum.[6]

History of Vaccine Hesitancy

Anti-vaccination sentiment rose shortly after the advent of vaccination, beginning with Edward Jenner's smallpox vaccine in England at the turn of the 18th century. Smallpox outbreaks led to vaccination campaigns in the United States, stimulating the founding of the Anti Vaccination Society of America in 1879.[7] During a smallpox outbreak in Cambridge, Massachusetts in 1902, the US Supreme Court ruled in support of the city's right to mandate the vaccine in the context of a local outbreak, setting a precedent for the role of the government in public health emergencies.[7]

As the smallpox vaccine was demonstrating remarkable success around the world, the Salk polio vaccine was brought to market to prevent the devastating impact of polio on children. The polio vaccine was also extraordinarily successful, leading to the eradication of wild-type polio from most nations around the globe. However, the early roll-out of this vaccine was not without missteps. In 1955, Cutter Laboratories produced some batches of polio vaccine that were not inactivated, therefore containing live polio virus and leading to over 200 cases of paralysis and 10 deaths. The "Cutter Incident" led to many lawsuits against vaccine manufacturers and ultimately inspired the creation of an improved process for the oversight and regulation of vaccine manufacturing.[8]

During the 1970s and 1980s, the Diphtheria Pertussis Tetanus (DPT) vaccine was in widespread use. This vaccine was associated with more substantial side effects than those associated with the Diphtheria Tetanus acellular Pertussis (DTaP) vaccine that we use today. Along with the known side effects of DPT, there were a number of unsubstantiated reports of neurologic damage related to the vaccine, leading to an increase in lawsuits targeting vaccine manufacturers.[7] These lawsuits ultimately chased several companies from the market, and, by 1984, there was only one US company still manufacturing DPT. A growing concern for vaccine shortages led to the creation of the National Childhood Vaccine Injury Act (NCVIA) in 1986. This act paved the way for improved vaccine program regulatory processes, including the National Vaccine Injury Compensation Program (NVICP) in 1988, the Vaccine Adverse Events Reporting System (VAERS) in 1990, and the creation of Vaccine Information Statements (VIS) in 1991.[9]

Then, in 1998, the anti-vaccination movement was ignited by the publication of a study in *The Lancet* authored by former British physician Andrew Wakefield that proposed a link between the Measles Mumps Rubella (MMR) vaccine and autism.[7] This paper was subsequently retracted by *The Lancet* due to falsification of data and financial conflicts of interest, and Wakefield was barred from practicing medicine in the UK.[7] Unfortunately, the damage was already done. This now infamous article unleashed a new wave of anti-vaccination sentiment due to unsubstantiated fear that this vaccine would cause autism, leading to a decrease in uptake of immunizations and,

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ultimately, a number of vaccine-preventable disease outbreaks around the world. Celebrities and media became an echo chamber for anti-vaccination sentiment. During the years following the Wakefield article, anti-vaccine legislation targeting school vaccine mandates led to a trend toward more non-medical exemptions from vaccination.[10] Despite a declaration of measles eradication in the US in 2000, worsening vaccination coverage led to outbreaks of measles, such as the Disneyland outbreak in 2015. By 2019, the US experienced the most cases of measles since 1992, indicating a growing problem that showed no signs of relinquishing. In the wake of the various measles outbreaks, several states (California, Maine, New York, and Connecticut) passed legislation to eliminate non-medical exemptions, joining West Virginia and Mississippi as the only states without non-medical exemptions. However, there are still 44 states that allow non-medical exemptions from vaccination.

Historically, the emergence of a dangerous communicable disease has been largely met with widespread support for the corresponding vaccine. For example, families lined up with their children to get the polio vaccine in the 1950s. The COVID-19 pandemic has proved to be an anomaly in this respect, as this vaccination was met with a great deal of skepticism, and vaccine confidence has waned over the course of the pandemic.

Impact of COVID-19 on Vaccine Confidence

Leading up to the COVID-19 pandemic, there was growing evidence that vaccine hesitancy was gaining a foothold as a pivotal issue in US politics. For example, in 2018 anti-vax political action committees (PACs) played a large role influencing which candidates were on the ballot, and their lobbying prevented the passage of legislation intended to strengthen public health vaccination programs in many states.[11] A 2018 study demonstrated that Russian Twitter bots and trolls were amplifying anti-vaccine messaging to fuel the fire and erode vaccine confidence during that political cycle.[12] Over the subsequent year, it became clear that social media giants, such as Facebook and YouTube, were being used to spread misinformation and propaganda about vaccines, laying the groundwork for the public health misinformation campaigns that plagued the COVID-19 pandemic.[13]

By the end of 2020, the first COVID-19 vaccine – created using cutting edge messenger RNA technology but with the unfortunate name of "Operation Warp Speed" – was rolled out in the US. As with polio in the 1950s, many people were clamoring to get the vaccine; however, many others met this vaccination with skepticism and mistrust, citing the speed of development and approval, concern about "new" technology, and fear of long-term side effects as rationale for delaying or refusing the vaccine. A study published in October 2021 by the Kaiser Family Foundation found that only 27% of parents were willing to get their 5- to 11-year-old vaccinated as soon as it was available for that age group.[14] Studies have demonstrated an increase in overall childhood vaccine hesitancy over the course of the COVID-19 pandemic in addition to hesitancy regarding the COVID-19 vaccine specifically.[15,16]

Notably, the face of the anti-vaxxer has changed during this pandemic. There is a striking difference between populations regarding uptake of COVID-19 vaccine, with Democrats, college graduates, urban residents, women, and people age 65 and up being far more likely to receive the vaccine than Republicans, rural residents, men, and people age 30-49.[14] The pandemic and political climate have stimulated the "anti-vax movement's radical shift from crunchy granola purists to far-right crusaders."[17] There are also significant sociodemographic disparities in intention to vaccinate, with caregivers of Black children and from rural and disadvantaged

neighborhoods being more hesitant to vaccinate their child against COVID-19.[18] Furthermore, different vaccines engender hesitance in different populations. For example, people who refuse the MMR vaccine are not the same as the ones refusing the COVID-19 vaccine, and the principles impacting this decision are different.[19]

Under-Immunized Populations

In order to establish comprehensive, evidence-based interventions to improve childhood vaccine uptake, it is crucial to understand the influence of sociodemographic and political disparities as well as the populations directly impacted: children and their surrogate decision-makers (usually the parents). Vaccine hesitant parents typically fall into one of four categories: 1) no specific objection but concern due to external factors such as media; 2) concern about specific vaccines e.g., MMR or COVID-19; 3) concern about the timing of the recommended vaccine schedule; or 4) opposed to all vaccines (including for religious or philosophical reasons). Different interventions will have varying success with each of these groups of caregivers, so a comprehensive approach should include a variety of culturally sensitive strategies aimed at all groups.

The result of the vaccination decision that is in the hands of the surrogate decision-maker is the potential for a child to be underimmunized. Like other populations in society warranting special protections, such as disabled persons, the socioeconomically disadvantaged, racial and ethnic minorities, children in foster care, and the underinsured, underimmunized children are a vulnerable population.

Vulnerable status stems from economic, cultural, ethnic, or health characteristics that lead to disparate healthcare access and outcomes.[20] In the case of underimmunized children, there are four main contributors to vulnerable status. First, they have surrogate decision-makers that are making inadvisable decisions on their behalf. Regarding the COVID-19 vaccine, there is some evidence that vaccine confidence is related to practice of other preventative behaviors; so, it can be extrapolated that inadvisable medical decisions may extend to other areas of health.[21] Second, underimmunized children have a relative immunodeficiency compared with their appropriately immunized peers; they are at greater risk for serious, life-threatening, vaccine-preventable diseases such as measles, pertussis, pneumonia, and meningitis. Third, they are at higher risk for certain cancers, specifically HPV-related malignancies such as cervical and oropharyngeal cancer as well as hepatocellular carcinoma related to Hepatitis B. Finally, they have decreased access to adequate medical care due to a significant increase in pediatric practices dismissing or refusing to care for these families.[22] This practice can force underimmunized patients to cluster at practices that will accept them, which can put these practices at risk for disease outbreak, or transition to a “vaccine friendly” provider who is unlikely to promote vaccination by catering to the needs of vaccine hesitant families.[23] The decrease in access to adequate healthcare is often compounded by recurrent adversarial confrontations with the healthcare system experienced by vaccine hesitant parents, further leading them to avoid contact with conventional healthcare providers.

Along with children and their parents, there are other key stakeholders that are affected by the underimmunized child. They include populations at risk of serious illness from vaccine-preventable diseases, other children at school or in the waiting room of a practice, teachers, and healthcare workers. An ethical analysis of vaccine hesitancy should balance the best interest of the patient with that of society, autonomy of patients and preferences of parents, emerging

autonomy of adolescents, potential for harm from the vaccines and harm from being underimmunized, protection of the vulnerable, and distribution of limited resources.

Vaccine Controversies

There are several common vaccine concerns that have strong evidence to discredit them. For example, the evidence is strong that there is no causal link between MMR or thimerosal, the mercury-based preservative, and neurodevelopmental disorders such as autism.[6] Studies have failed to show evidence linking autoimmune disease and vaccines. Aluminum adjuvants are safe and effective. And while certain vaccinations, such as varicella, rubella, and hepatitis A are made by growing viruses in fetal embryo fibroblast cells first obtained in the 1960s, the Vatican has issued a statement on immunization promoting the use of these vaccines.[24]

Some vaccine hesitancy is related to the sheer number of vaccinations and the young age of children upon initiation: the "too many too soon" concern. In the United States, the number of diseases recommended for prevention by childhood immunization has increased from five in 1960 (smallpox, polio, diphtheria, tetanus, and pertussis) to 17 in 2022 (including COVID-19).[25] During the same time period, improvements in vaccine science led to a decrease in the total number of antigens contained in those vaccines from >3000 in five vaccines to <200 in the 17 current vaccines,[25] which is thought to be responsible for the significant decrease in side effects with the current recommended vaccine schedule. Further, the recommended schedule was studied at the suggested ages to maximize benefit while minimizing harm; any deviation from the evidence-based schedule is likely to come at the cost of reduced immune response.

Approach to Vaccine Hesitancy

A comprehensive approach to vaccine hesitancy requires intervention at many different levels and must be informed by an evidence-based understanding of the risks and benefits of immunization as well as techniques to improve uptake at the individual and population level. Upstream approaches are the most effective strategies to improve vaccine uptake but tend to be the most difficult to execute. At the state level, the single most effective strategy has been school and childcare mandates for vaccines. Vaccines required for school entry have uptake exceeding 94%, and only 2.5% of children had an exemption for at least one vaccine.[26] Another upstream approach, the elimination of non-medical exemptions, has led to a significant decrease in the number of children entering school underimmunized.[27] Finally, targeting access for immunizations to underserved communities with disparities in vaccine uptake can help support health equity.

At the practice level, a formalized protocol for the management of underimmunized patients and families can improve uptake and protect both patients and staff. This protocol should be transparent to families and staff from the establishment of the provider-patient relationship. Potential policies for the underimmunized patient can include mandating regular well visits, eliminating walk-in visits, masking the patients and accompanying caregivers, avoiding the waiting room when sick, and using a refusal to vaccinate form. Practices can maintain a registry of underimmunized patients, which can be used in the event of a regional outbreak to notify families of the heightened need for vaccination. Along with practice-level policy changes, practices can engage in quality improvement initiatives to improve vaccination coverage, including the use of registries to identify gaps in care, standing orders, and provision of vaccines at all opportunities.

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Some providers refuse to see underimmunized patients or dismiss them from their care, a practice that is both controversial and ethically problematic.[28] While dismissal of vaccine refusing families does have the benefits of reducing the number of underimmunized children in the office and waiting room while also decreasing the time and potential frustration of working with families that are not following medical guidance, there is no evidence that this practice improves vaccine uptake. However, this practice does lead to mistrust and decreased access to healthcare, leading to increasing health inequities and vulnerable status. Furthermore, this is a missed opportunity for trust building, continued education about vaccination, and preventative counseling in the event of a disease exposure or outbreak.

At the provider level, it is most beneficial to continue to engage with a hesitant family, recognizing that they have the potential to change their minds about immunization over time. Many studies have demonstrated the importance of the trusted provider's recommendation on the immunization decision.[18] Providers should work hard to establish rapport, trust, and a therapeutic alliance that is not solely focused on the immunization decision, but the whole patient. Families want providers to listen carefully, respectfully, and non-judgmentally to their concerns, and providers should elicit the reasons and supporting evidence for these concerns. Information gathering can help the provider to better understand what type of hesitant parent they are dealing with, which can inform the approach. For instance, parents who have no specific objection but are concerned due to word-of-mouth are often amenable to a strong provider recommendation, while parents who are opposed to all vaccines tend to not be as flexible. The provider should educate the surrogate decision-maker in a culturally sensitive manner about what is known (and not known) about the risks and benefits of immunization, including correcting misperceptions and misinformation, providing resources, and sharing real life stories. It can be helpful to directly compare the risks of the vaccine with the risk of being unimmunized. The provider can also work with the family, using shared decision-making, to vaccinate the child at a different pace than the recommended schedule to engender trust and confidence.

There is growing evidence for several specific techniques to improve vaccine uptake. Providers can use a presumptive approach to offering vaccines, stating "your child is due for her vaccines today," rather than an opt-in approach, such as asking "what do you think about doing vaccines today?" Another technique is motivational interviewing, where providers can guide conversations in a non-confrontational, non-paternalistic manner to lead patients and caregivers to be internally motivated to follow recommendations.[29] Finally, persistence after initial resistance can demonstrate the importance of vaccination for families and influence their decision.[30] Providers should strive to make a strong recommendation and then persist in their recommendation later during the same encounter but also over time at future encounters, knowing that with time and trust, many families will change their minds.

Conclusion

Vaccination programs have been the victims of their own overwhelming success, as fading memories of terrifying vaccine-preventable diseases are accompanied by intensifying vaccine hesitancy and mistrust. The false equivalency between the severity of vaccine side effects and the diseases they are meant to prevent opens the door for vaccine hesitancy, which has been amplified by social media, political agents, immoral influencers acting in bad faith, and the COVID-19 pandemic.

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Vaccine hesitancy is influenced by sociodemographic factors, highlighting the importance of developing culturally sensitive approaches for different populations, which must be informed by an understanding of the different types of vaccine hesitant parents as well as the vulnerable status of underimmunized children. Strategies to improve immunization uptake can include upstream approaches, such as school mandates and elimination of non-medical exemptions, practice-level approaches such as thoughtful protocols for the management of underimmunized children and their families as well as quality improvement initiatives, and provider-level techniques such as the presumptive approach, motivational interviewing, and a strong and persistent recommendation. Protecting children from vaccine-preventable diseases is a challenging yet admirable endeavor that requires a multi-level strategy with a focus on health equity and the protection of the vulnerable.

Dr. Miller can be contacted at jonathan.miller@nemours.org

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