

Adherence to Immunization: Rebuttal of Vaccine Hesitancy

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Abstract

Immunizations have been saving the lives of millions of people since they were first used by Edward Jenner in 1796, and new vaccines are being developed all the time. Hopefully, a new vaccine for coronavirus disease 2019 (COVID-19) will be developed in the near future, and perhaps even one for human immunodeficiency virus. Although the effectiveness of vaccinations has been proven over the years and adverse effects to currently available vaccinations are extremely rare, many people continue to defer immunizations for themselves and their families. According to the World Health Organization (WHO), this phenomenon, known as “vaccine hesitancy,” is a major public health problem globally. This review summarizes the unproven adverse effects of various vaccines and stresses the importance of enforcing vaccination policies to minimize vaccine hesitancy. Every effort should be made to improve existing vaccines and to produce new ones, according to carefully designed scientific preclinical and clinical trials. This is particularly important in today’s era, in light of the global transparency regarding vaccination development, and the potential for future pandemics such as COVID-19.

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Introduction

Over the past century, life expectancy has increased from around 40 years to more than 80. Clearly, this increase cannot be attributed to genetic changes in the population; rather, it is primarily due to 3 factors: understanding the importance of hygiene, the use of antibiotic and antifungal drugs, and the mass use of vaccination against infectious pathogens of viral and certain bacterial origin [1]. In the past, millions of children worldwide died due to a number of infectious diseases, for which vaccinations are now available, thereby preventing the tragic consequences of these diseases. The World Health Organization (WHO) recently reported that from 2000 to 2017, more than 21 million deaths were prevented, thanks to the measles vaccine [2], and aggressive immunization programs worldwide have eradicated small pox [3]. Vaccines are highly effective for conditions that were once greatly feared, including polio, whooping cough, and rubella. Nevertheless, for some highly pathogenic viruses, such as human immunodeficiency virus and the most recent coronavirus disease 2019 (COVID-19), the search for an effective vaccine is ongoing.

Since the first smallpox inoculation by Jenner in 1796, dozens of different vaccines have been developed. Today, there are 2 main types of vaccinations: life-attenuated vaccines, which use a weakened form of the disease-caus-

ing organism, and inactivated (or killed) vaccines, which consist of virus particles, bacteria, or other pathogens that have been grown in culture and then lose disease-producing capacity. As the latter are less immunogenic, they are conjugated to adjuvants to enhance their immunogenicity [4].

However, there is an increasing phenomenon, called vaccine hesitancy, which is preventing the full eradication of conditions such as polio and measles. The SAGE (Strategic Advisory Group of Experts) Working group on vaccine hesitancy has defined this as the refusal of or delayed acceptance of being vaccinated despite availability [5]. It is “complex and context specific, varying across time, place and vaccines. It is influenced by factors such as complacency, convenience and confidence.” [5, p. 4163]. Unfortunately, vaccine hesitancy is becoming widespread worldwide. According to the WHO, vaccine hesitancy is one of the 10 major health threats worldwide [6].

Effective vaccination programs are being administered worldwide against a number of common conditions, including *Haemophilus influenzae*, varicella, rotavirus, and papillomavirus. Nevertheless, “vaccine hesitancy” is undermining such programs, leading to outbreaks of conditions that were close to being eradicated, such as measles.

This review provides an overview of the various unproven adverse effects of different vaccines that contribute to vaccine hesitancy and stresses the importance of vaccination policy enforcement so as to minimize hesitancy. It also explores the potential impact of vaccine hesitancy with regard to COVID-19, once an immunization is developed.

Adverse Reactions to Vaccination

Since the first administration of vaccinations, many true and false adverse reactions have been reported [7]. Reported side effects include local pain and erythema at the injection site, high fever, and irritability. However, reports of developing multiple myeloma after hepatitis B vaccination or autism following measles, mumps, and rubella (MMR) immunization have not been scientifically substantiated [7]. Like any medical product, including vaccines, some negative events may occur, even when there is a huge overall positive effect and benefit. Historically, 2 major tragedies have occurred due to defective vaccine production. In 1929, *Mycobacterium tuberculosis* was injected instead of the attenuated *Mycobacterium bovis* (BCG), causing the death of more than 50 children [8].

The second tragedy occurred in 1955 when a non-fully inactivated poliovirus vaccine was given to more than 100,000 children, causing several cases of paralysis. Aside from these 2 tragedies, it has been noted that 1 in 2.5 million oral polio vaccinees may develop paralysis, and the original rotavirus vaccine was associated with intussusception in 1 in 100,00 vaccinees [9]. As a result, all of the serious adverse reactions are now well documented as potential side effects for a number of different vaccines. Minor reactions that can occur quite often have also been noted, such as local injection site pain and swelling at the injection site accompanied by fever. Very high fever and convulsions are rare complications.

There are some contraindications to vaccination, as with any other medication. Severe allergic reaction to a previous vaccine of the same kind is the main one [10]. Diphtheria, pertussis, and tetanus (DPT) immunization in children with progressive encephalopathy is also a contraindication for vaccination [11].

In addition, special precautions should be taken when administering vaccinations to patients with immune deficiency primary or secondary to chemotherapy, or to patients after hematopoietic stem cell transplantation. High-risk patients should not receive live-attenuated vaccine until at least 2 years have passed since transplantation with no evidence of graft versus host disease, and after all immunosuppressive drugs have been stopped [12]. Live-attenuated vaccines are also contraindicated in patients with primary immunodeficiency, especially in whom a T-cell defect exists.

There is no doubt that the vaccination benefits outscore the very small number of proven adverse reactions. Nevertheless, the last few decades have seen the rise of several groups campaigning against vaccination. Speculation regarding the association between immunization and autism and autoimmune phenomena has led to an increase in vaccine hesitancy among the general population, mainly in the Western world.

Unproven Reaction Leading to Vaccine Hesitancy

Reducing the level of vaccine hesitancy is a critical component for improving public health. To better understand this misconception regarding vaccination, the reports linking autism and autoimmunity to vaccination must be carefully examined. The autistic allegation started in 1998 with an article in *The Lancet* by Wakefield and colleagues [13] describing 12 children with autism and behavioral changes linking those changes to the MMR

vaccine. The article was subsequently found to be fraudulent, with false data [14]; it was discovered that Wakefield had received almost half a million pounds from a law firm that claimed an association between autism and the vaccination [14]. These facts led to the paper being retracted from *The Lancet*. However, the original paper had received so much media coverage, that it is hard to find a parallel case in the history of medical science with such potential for damaging public health [15]. A recent meta-analysis involving more than 1.2 million children found no relationship between autism and MMR, nor with any of the vaccine components [16, 17]. Although all scientific data point to no association between the MMR vaccine and autism, unfortunately, several anti-vaccine groups continue to advertise and insist that such an association exists [18]. These groups have cited numerous anecdotal and coincidental cases for which there are other explanations when closely examined scientifically.

The last decade has seen a marked increase in the number of allegations suggesting a correlation between autoimmune manifestations and vaccination [19]. Several proposed mechanisms for such an association have been discussed, including molecular mimicry by which viral antigens trigger an immune response against autoantigens [20], and the vaccine acting as a bystander that releases self-antigens from host tissue, thereby activating autoreactive T cells [21]. However, to date, no scientific findings have been found to support either of these proposed mechanisms. Still, a few very rare cases of autoimmune syndrome have been found to be associated with specific vaccines [22]. Guillain-Barre syndrome was noted in 1 out of 100,000 influenza vaccinees [23], and a possible link with idiopathic thrombocytopenia purpura and MMR vaccine has also been suggested [24]. Several large studies have debated the possible associations between the hepatitis vaccine and diabetes mellitus, and multiple sclerosis with the human papilloma virus vaccine [25]. Over the years, several rare anecdotal reports of various autoimmune manifestations have been linked to vaccination, but they have not been followed in large-scale studies.

Ten years ago, a new syndrome “autoimmune/inflammatory syndrome induced by adjuvants” (ASIA) was proposed as a possible link between vaccines and autoimmunity [26]. It was suggested that adjuvants, mainly aluminum (added to vaccines to boost the immune response), can lead to chronic activation of the immune system, eventually causing a variety of autoimmune manifestations [26]. According to this theory, the autoimmune conditions can develop even 20 years postvaccination. As

the symptoms attributed to ASIA are very broad and ill-defined, most authors refute the existence of this syndrome [27]. Furthermore, in a study that included more than 18,000 people who underwent allergic immunotherapy (which contains high amounts of aluminum), a lower rate of autoimmune disorders was found when compared to a control group [28].

Vaccine Hesitancy and COVID-19

The importance of vaccination and the negative effect of vaccine hesitancy were observed recently during a measles outbreak affecting more than 600 children in a Jewish orthodox community in New York City [29]. Many of the patients needed treatment in an intensive care unit. Vaccination had not been recommended within this community, although in other parts of the city where vaccinations were administered according to a regular vaccination schedule, almost no cases were reported!

This same hesitancy to observe precautions against infection and contamination during the COVID-19 pandemic has been observed worldwide [30]. To date, several additional studies have clearly demonstrated that vaccine hesitancy is an attitude that reflects a lack of trust in medical research and the authorities [31]. Although a COVID-19 vaccine has not yet been found, when it is, its implementation may be even more challenging due to the plethora of social media already claiming that a COVID-19 vaccine will have a number of negative effects ranging impacting everything from health to society and government [32]. Indeed, several other recent studies have shown that many people will refuse a COVID 19 vaccine. Current estimates include 20% declining it in the USA [30], while in Australia, only 4.9% [33] are against the vaccine. These numbers may, in part, reflect the level of confidence people have in their respective governments [31]. While there is no question that vaccines are a critical component of public health, many vocal groups are extensively using social media, ignoring the science, and continue to promote the idea that vaccinations cause more harm than good [34].

The analogy is clear. In some communities (like the one in which the measles outbreak occurred), nonadherence to the recommendations of local health authorities or the international ones (WHO) led to an extremely high incidence of COVID-19 with both high morbidity and high mortality [35].

A second point to consider is that in light of the already evident lack of trust regarding vaccination, the rush to

develop one for COVID-19 must be accompanied by very clear, solid, and unquestionable investigation and research. China [36] has already initiated vaccination for COVID-19 without having conducted the important studies needed to prove its safety and effectiveness, and Russia has just announced a vaccine, about which very little is known [37]. Rushing the vaccine development may lead to some serious adverse effects that will compound current vaccine hesitancy, not only for this specific disease but for all diseases!

Conclusion

Vaccines have saved hundreds of millions of infants and children from death over the last 100 years; hence, they represent the most important health prevention measure worldwide. In comparison, the huge technological advances in the medical field (such as innovative diagnostic techniques and medical procedures such as transplantations) have had a relatively minor impact on global health. It is therefore clear that vaccination should be encouraged, together with a scientific methodology for tracking and following possible side effects. In recent years, the promulgation of vaccine hesitancy, particularly via social media, has led to an alarming decrease in vaccinations with the potential of infectious outbreaks worldwide [38].

Every effort must be made to decrease the level of vaccine hesitancy by educating the public on the benefits of immunization, with clear explanations that debunk the misconceptions being spread. Furthermore, the beneficial effects of vaccination versus the adverse effects if not implemented, need to be clearly conveyed to all parties involved in the administration of immunizations. It has been found that inconsistent communication from public health experts and elected officials regarding health risks directly leads to an increase in vaccine hesitancy [32]. Public information campaigns aimed at increasing

confidence in vaccinations may be effective in reducing hesitancy. In some situations, increased confidence in immunization may be achieved by improving the amount and quality of information disseminated to health-care providers, local authorities, and religious leaders. Respectful campaigns on social media and public programs, targeted at groups known to be more resistant to vaccination, could increase vaccine acceptance [39]. In a systematic review of 166 peer-reviewed journals, it was found that the most effective interventions employed multiple strategies [40]. These included increased vaccination knowledge, engaged religious leaders, improved access to vaccination, and sanction against no vaccination [40].

Reducing vaccine hesitancy is particularly important during this stage of human history, when the global community is facing the enormous negative health and economic impact of COVID-19. Finding a vaccine (after conducting appropriately controlled clinical studies) will help solve the global health problems caused by this virus and will be just as important as the small pox, polio, and other vaccines were in their day. It is clear that if vaccine hesitancy continues to propagate worldwide, it will not only negatively impact health and quality of life but could potentially impede the development of future vaccines. Hopefully, the implementation of targeted multimedia campaigns, combined with solid vaccine research, will reduce the hesitancy toward a licensed COVID-19 vaccine, once developed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Author Contributions

Both authors have written the paper and discussed its contents.

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